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BROAD SPECTRA NUTRITIONAL SUPPLEMENTATION OF MAINTENANCE HEMODIALYSIS PATIENTS

by

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A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE IN NUTRITION

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FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled "Broad spectra nutritional supplementation of maintenance hemodialysis patients" submitted by Ferne Alice Lazarenko, B.Sc., in partial fulfillment of the requirements for the degree of Master of Science in Nutrition.

Elizabeth A. Gonnaid
SUPERVISOR

DATE: August 27, 1975

DEDICATION

This thesis is dedicated to the women, men, and children whose lives depend(ed) on hemodialysis, and to their families. Their profound influence on the personal philosophy and professional knowledge of the author, and their generous contribution to the completion of this study will always be deeply and gratefully remembered.

ABSTRACT

A 20-week study was conducted to assess the effect of broad spectra nutritional supplementation on energy, protein, and iron status of maintenance hemodialysis (MHD) patients. Eleven male Caucasian patients, 22-60 years, who had been on hemodialysis longer than 6 months and were judged medically stable served as subjects. The patients were either hospital outpatients or on home dialysis, and all but 1 was routinely dialyzed for 5-8 hours, 3 times/week.

A broad-spectra nutritional supplement (MJ 7014)* was used to supplement the ad libitum intakes of 4 patients. These patients also took vitamin supplements in pill form. MJ 7014 was consumed by all experimental subjects for at least 11 weeks and by 1 subject for 20 weeks. Seven patients were not supplemented with MJ 7014 but did take placebo pills in place of the vitamins.

Total energy intake of the control group remained fairly constant throughout the study at approximately 2100 kcal/day, but varied in the experimental group from 2500 to 3300 kcal/day, due to variable intakes of MJ 7014. The control group gained approximately 1 kg of body weight. This was accompanied by a slight decrease in per cent body fat, skinfold thickness, and cross-sectional fat area of the arm. The experimental group gained about 3 kg body weight, while experiencing a reduction in cross-sectional fat area of the arm and a significant reduction ($P < 0.05$) in per cent body fat and skinfold thickness. Therefore, weight gained by both groups was not deposited as body fat.

*Mead Johnson Product 7014

Total protein intake ranged from 77-84 g and 89-103 g/day in the control and experimental groups, respectively. Both groups were dialyzed 3 times/week and were able to metabolically handle these higher protein levels without adverse effect. Protein status of both groups was found to be adequate, as assessed by lean body weight, arm-muscle circumference, percentage of hair in the anagen phase and serum albumin. A gradual reduction in blood urea nitrogen (BUN) levels in both groups would seem to indicate endogenous use of BUN for tissue protein synthesis. In spite of being subjected to the trauma of surgery and inter-current infection, protein status of the experimental group did not deteriorate. This finding may have been due to their high intake of protein.

Both groups obtained 12-14 mg of iron/day from dietary sources. Consumption of MJ 7014 by the experimental group increased their daily iron intake by 1-7 mg. Simultaneous administration of parenteral iron obscured any benefits which might have been derived from oral supplementation of iron. The experimental and control groups were anemic but not iron deficient, as demonstrated by below normal levels of hemoglobin and hematocrit, but normal levels of serum iron, total iron binding capacity, and per cent saturation of serum transferrin.

The use of MJ 7014 as a supplement to an ad libitum diet was limited by several factors such as excessive sweetness and amount of fluid needed to dissolve the powder. High cost could also be a consideration. Subjects in the present study underwent dialysis 3 times/week and were able to handle relatively generous levels of protein with no adverse effect. Many were of normal weight and had adequate stores of body protein and fat while consuming nutritionally adequate diets ad libitum. Routine broad spectra supplementation would not be necessary

unless patients failed to consume a nutritionally adequate diet, were malnourished, or were subjected to much physiological stress.

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INTRODUCTION

"Primary aims of hemodialysis are to return patients who have end-stage kidney disease to society as soon as possible, to sustain their nutrition, body chemistries, and physical health at near normal levels, and, in many instances, to maintain them in a state satisfactory to receive a kidney transplant. These goals are sought at a minimum cost, time, and risk to the patient" (1).

To prevent the accumulation of the end products of protein metabolism as well as sodium, potassium, and water, maintenance hemodialysis patients are usually requested to limit their dietary intakes of these nutrients. While some dietary restriction is necessary due to terminal renal failure, severe dietary restriction may also limit patient adherence to the diet and unfavorably alter food habits, thus reducing the daily intake of many nutrients. Furthermore, the process of hemodialysis has been shown to non-selectively remove water soluble nutrients, as well as toxic substances, from the bloodstream of patients. Consequently, the nutritional status of hemodialysis patients is often compromised.

Patients dialyzed three times per week are able to consume fairly liberal diets. Many, however, continue to consume insufficient amounts of energy, restrict the quantity and quality of protein eaten, and avoid foods providing many vitamins and minerals for fear of becoming overloaded with sodium, potassium and/or fluid.

The object of this study was to provide maintenance hemo-

dialysis patients* with a broad spectra nutritional supplement and to assess the effect on energy, protein, and iron status by studying dietary intake, hair characteristics, and several anthropometric and biochemical parameters.

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* As patients approach the end-stage of chronic renal failure they exhibit clinical signs and symptoms of uremia, and are described as being "uremic". When less than 5% of total kidney function remains conservative treatment, including diet therapy, can no longer control the uremic state. Dialytic treatment must then be instituted, or death will ensue. Unless otherwise specified, this thesis relates to patients whose uremic state is regulated by maintenance hemodialysis.

LITERATURE REVIEW

THE NEED FOR ENERGY IN MAINTENANCE HEMODIALYSIS (MHD) PATIENTS

During the 1960's maintenance hemodialysis, and renal transplantation became possible, and dietary management of uremia was improved (2). Giordano (3) and Giovanetti and Maggiore (4) illustrated the value of diets containing adequate amounts of energy and low levels of high quality protein, for uremic patients not requiring hemodialysis.

Prior to beginning dialytic therapy, uremic patients may have carefully adhered to a diet restricted in protein and sodium content. Inadvertently these diets may also have been inadequate in calories, thus leading to the use of protein for energy and a depletion of body stores of protein (2, 5). Diets less restrictive in nutrients are often prescribed with the commencement of dialytic therapy. In spite of more liberalized diets and improved appetites, many patients continue to exhibit signs consistent with mild to severe energy deficiency (6). A physician may fail to prescribe a diet (5, 7), or the patient may fail to consume a diet containing enough energy. Patients may also experience intercurrent illness which can decrease appetite and ultimately energy intake.

Fish and co-workers (8) prescribed diets containing 1500-3000 kcal and 80 g of protein for 22 female and 24 male patients, prior to their discharge on home dialysis programs. All patients were dialyzed thrice weekly, using a Kiil dialyzer, and were followed for 6-42 months (mean 18 months). Energy intake of the patients varied, depending on age, sex, weight and activity. The "low stable 'dry-weight' value" during the training program was used as the initial weight. Weight remained unchanged in 4 patients, was lost by 1 patient, and was gained by 41 patients, when compared with the initial weight.

Of those who gained, 25 patients gained 1-10% more weight, 11 gained 11-20%, and 5 gained more than 20% (range 21-45%). Fish and co-workers concluded that when body weight was used as a criterion, these patients could be considered nutritionally rehabilitated.

Llach and co-workers (9) used MJ 7014* as the chief source of calories and dietary essential amino acids for 5 hemodialysis patients. The diet provided 4000 kcal, and 50 g of protein daily for 4 weeks. The researchers reported that MJ 7014 was well-tolerated; no significant change in body weight occurred; and nitrogen balance was positive in the majority of patients. An improvement in strength and well-being was reported by the subjects.

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* Mead Johnson Product 7014.

PROTEIN STATUS AND THE NEED FOR PROTEIN IN MHD PATIENTS

Introduction

Protein nutrition and the clinical use of diets for the treatment of chronic renal failure have been discussed (10-12). The ultimate goal is to determine the best dietary prescription and dialysate composition combined with sufficient dialysis to maintain as normal a state of nutrition as possible. The current trend is to use a more liberal diet (8, 11, 13).

Protein Status of MHD Patients

Protein intake

No "best" dietary level of protein and amino acids for patients requiring hemodialysis has been proposed (14), whereas 0.8 g of protein/kg body weight is recommended for daily consumption by healthy adults (15). The most frequently suggested level of intake for hemodialysis patients falls within the range of 0.75-1.0 g of protein/kg body weight/day (10, 12, 16-19). Approximately 0.63 g or 2/3 of the suggested protein intake should be of high biologic value (10, 14, 16-18). Diets providing this quantity and quality of protein should maintain neutral or positive nitrogen balance (10, 16, 18); minimize uremic symptomology (10, 14, 16, 18); and promote the use of endogenous urea for protein synthesis (14). According to MacKenzie (11), there is no evidence that 0.8-1.0 g of protein/kg body weight/day is deleterious, provided blood urea levels are maintained as low as possible and uremic symptomology is minimized.

Patients dialyzed 3 times weekly were prescribed a daily

intake of 80 g of protein by Fish and co-workers (8) and Pendras (13). A major portion of the protein prescribed by Fish et al. (8) was of high biologic value, whereas the protein quality was not specified by Pendras (13). For a man weighing 70 kg, this represents a daily protein intake of approximately 1.1 g/kg body weight. Fish and co-workers (8) found that this level of protein intake, combined with an energy level of 1500-3000 kcal resulted in nutritional rehabilitation of 46 home dialysis patients. They found an increase in body weight and serum albumin over a mean duration of 18 months. Pendras (13) recognized the long-term difficulties patients encounter following a 40 g protein diet. These difficulties include: lack of satiation, difficulty adhering to the diet, a feeling of fatigue, and failure to maintain an adequate nutritional status. Therefore Pendras conducted a "practical" study to determine patient acceptability of diets containing a more liberal intake of protein and the consequent effect on blood levels of urea nitrogen, creatinine, albumin, and globulin. One group of 14 patients consumed 80 g of protein daily and received thrice-weekly dialysis, whereas a second group of 25 patients consumed 60 g of protein daily and received twice-weekly dialysis. Pendras reported that both groups did well clinically, and that patients consuming the 80 g protein diet "voluntarily tolerated the inconvenience of additional dialysis for the reward of more food". He concluded that in maintenance hemodialysis therapy, the concern should be how much, rather than how little, protein and sodium can be consumed without harmful effect.

Urea utilization

Smith and Hill (14) investigated the ability of diets

containing an adequate level of energy and protein of high biologic value to produce biochemical and clinical improvement in hemodialyzed patients. They studied the level of urea nitrogen; total protein, albumin, and creatinine in blood of 1 normal volunteer, 2 non-dialyzed uremic and 3 hemodialysis patients, to determine the ability of these subjects to utilize urea for synthesis of plasma protein. The difference between the level of blood urea nitrogen on day 1 and day 21, the last day of the study, was determined. Blood was sampled previous to undergoing dialysis in order to eliminate any variation in levels of blood urea nitrogen due to the dialytic treatment. To study the extent of urea utilized for the synthesis of plasma protein, the nitrogen portion of urea was labelled. Urea was dissolved in water, divided into 3-4 portions and orally administered at meal-time on day 1. "A constant diet of a modified G-G type" was given, with milk and eggs providing the dialyzed subjects with 0.63 g of protein/kg body weight. Approximately 0.7 g of protein and 27-54 kcal/kg body weight was consumed by the 3 hemodialysis patients. Blood urea nitrogen decreased during the study, although body weight, plasma creatinine and serum protein (total and albumin) showed little change. Smith and Hill felt that the reduction in blood urea nitrogen was indicative of urea utilization for tissue protein synthesis. The incorporation of labelled urea into plasma protein and serum albumin was similar in the 3 hemodialyzed patients. Both the dialyzed and non-dialyzed uremic patients incorporated more isotopic nitrogen into plasma protein than did the 1 normal control subject. Smith and Hill concluded that hemodialyzed patients have the ability to utilize non-protein nitrogen, but to a lesser extent than the non-dialyzed uremic patient.

Other Factors Affecting Protein Status and the Need for Nitrogen

Nitrogen loss via effluent dialysate

Hemodialysis removes not only toxic materials that cause uremic symptomology, but also normal constituents of plasma, including amino acids, water soluble vitamins, and trace minerals. Unless these substances are replaced by dietary or pharmaceutical means, deficiency states may occur (20). Although protein is not lost during hemodialysis, because of their small molecular weight, significant quantities of amino acids are lost (7, 20). Factors influencing the amount of total alpha amino nitrogen removed during hemodialysis include: flow rate of blood, volume of dialyzing fluid, surface area and porosity of dialyzer membrane, and duration of dialysis (21, 22).

Several investigations have been conducted to determine amino nitrogen losses during hemodialysis (7, 16, 20, 22-24). A varying number of subjects have been dialyzed with different machines, for varying lengths of time and findings have been expressed in various ways, such as grams of mixed protein, alpha amino nitrogen, amino acids, free amino acids, or bound amino acids. For these reasons it is difficult to generally state the amount of nitrogen which might be lost through dialysis.

Total amino acids: Comty (7) reported dialyzer losses of total amino acids equivalent to 20 gm of mixed dietary protein per week, in an unspecified number of patients who were dialyzed 28-32 hours per week. Rubini and Gordon (20) studied the loss of amino acids into effluent dialysate of 14 adult maintenance hemodialysis patients being dialyzed 1-3 times per week, for 8-12 hours, using a

Western-gear modified Kiil machine. If dialysis occurred during meal-time, the patients were given their usual meal and post-prandial samples were taken. The clearance of 18 amino acids into effluent dialysate was determined for each patient 30 minutes, 6 hours, and 12 hours following commencement of dialysis. A mean loss was reported for each amino acid from all 12 dialytic treatments. Rubini and Gordon observed consistent and significant losses of amino acids equivalent to about 4.8 g of protein per dialysis. A loss of essential amino acids of up to 50% of the minimum daily requirement (MDR) for the adult occurred (20).

Aviram and co-workers (23) determined the effluent losses of 21 amino acids and other nitrogenous substances, including urea and creatinine, in 14 patients dialyzed with a Western-Kiil machine. All patients were fasted overnight and during the collection period. Amino acid losses were determined over a 3 week interval. Collection periods ranged between 4-65 minutes, and data was extrapolated to 8 hours, the usual duration of hemodialysis. The loss of essential amino acids was found to be less than 20% of MDR, as defined by Rose. Larger losses of 36, 44 and 48% of MDR occurred for valine, lysine, and threonine, respectively (23). The discrepancy between the loss of essential amino acids reported by Rubini and Gordon and that reported by Aviram and co-workers, may be due to differences in the dialyzer used and/or method of collecting and determining the amino acid losses.

Total alpha amino nitrogen: Total alpha amino nitrogen losses via effluent dialysate were determined by Ginn et al. (16) in 2 of 4 anephric male patients participating in a 32-day nitrogen balance study. The 2 patients consumed diets containing 18 g of high

quality protein, and 4 g of low quality protein, and underwent two 6-7 hour dialyses per week with a twin-coil dialyzer. About 20 ± 2 g of total nitrogen, and 2.4-3.5 g of alpha amino nitrogen was recovered per dialysis.

Free and bound amino acids: Bound amino acids, as well as free amino acids are removed during dialysis. Kopple and co-workers (24) found a mean loss of 6.3 g (range 4.5-7.7 g) of free amino acids and a mean of 3.7 g (range 2.4-5.2 g) or bound amino acids in 7 fasting male patients whose blood was dialyzed twice weekly for 10-11 hours with a glucose-free bath, using a Kiil dialyzer. Approximately one-third of the free amino acids removed were essential amino acids. They also noted a greater removal of free amino acids when the patients received food during dialysis, and when a glucose-free dialysate bath was used. Of the 19 amino acids found in bound form, less than one-fifth were essential amino acids. Giordano and co-workers (22) studied the loss of 20 amino acids in 3 patients who consumed 0.7-1.0 g of protein per kilogram per day, and who were dialyzed for 6 hours every 4 days with a twin-coil artificial kidney. Total loss of these 20 nitrogenous substances ranged from 2.3-3.3 g per hour, with 2-3 times more bound than free amino acids recovered. Giordano and co-workers concluded that between 14-20 g of amino acids, including peptides, are lost per 6 hour dialysis.

The effect of infection

The presence of an infection may influence the nutritional status of an individual. WHO (25) has said that "the quantitative effects of infections on the protein needs of an individual cannot be

stated, since they are likely to vary with the frequency, severity, and nature of the infection and other host factors, including nutritional status". Acute infections induce depletion of body nitrogen by firstly reducing protein intake, due to anorexia and/or therapeutic practices; and secondly, by increasing adrenocortical activity which normally causes an increase in urinary nitrogen excretion. Patients with renal failure are also known to be more susceptible to infection (26).

Shinaberger and Ginn (27) reported elevated levels of blood urea nitrogen, and gradually declining levels of serum albumin in 1 male patient who developed a low-grade fever and pericarditis, and in 1 male patient who developed duodenitis and transient hemorrhage. They observed that diets containing 0.75 g of high biologic value protein/kg body weight will permit nitrogen equilibrium in patients dialyzed twice-weekly but not suffering from infection. The finding of decreased levels of serum albumin led Shinaberger and Ginn to conclude that this level of protein intake does not provide sufficient reserve to accommodate excessive body catabolism during periods of stress. Infection is also known to cause reduced levels of serum transferrin and total iron binding capacity, according to Ooi and co-workers (26). Quoting the work of Jarnum and Lassen, these authors state that slightly increased turnover rates of serum albumin and transferrin are seen during states of infection. Ooi et al. concluded that more research is necessary to investigate the possible role of serum transferrin in host defense and resistance to infection in patients with chronic renal failure (26).

Giordano and co-workers (22) used the concentration of plasma amino acids to study the effect of infection on the protein

status of hemodialysis patients. They compared the plasma concentration of 21 amino acids in 5 normal subjects, with 2 groups of hemodialysis patients, following a 12 hour fast. The hemodialyzed subjects usually ate "liberal" diets containing 0.7-1.0 g of protein/kg body weight/day. The first group of 5 hemodialysis patients were ambulatory and were described as "doing very well". The second group of 3 hemodialysis patients were hospitalized with signs of infected wounds at the site of shunt implantation. In both groups of patients, the amino acid profile was not completely normal. The group of ambulatory patients had fairly normal, or high levels of plasma amino acids, including the essential amino acids. Fairly normal levels of plasma amino acids were also found in the group of hospitalized patients, except for slightly reduced levels of methionine and isoleucine. Giordano et al. felt that the high protein intake had "counterbalanced the tendency to deplete amino acid pools in infection". Furthermore, "once infection starts things get worse at rather a fast rate. Reduced appetite, increased catabolism and a shift in protein synthesis with an enhanced formation of globulins . . . cause the patient to go downhill." Giordano and co-workers concluded that low protein diets are contra-indicated in patients subject to frequent dialysis. They suggested that hemodialysis patients be prescribed diets containing a normal intake of protein.

Coles (28) described the effects of inter-current infection on body composition of 2 hemodialysis patients who were receiving a 50 g protein diet. One patient had an infected pelvic hematoma, whereas the other patient had jaundice and abdominal sepsis. With infection, body weight, body fat, and lean body weight were decreased

in both patients.

The effect of surgery

Surgery, as well as fever, is a catabolic state which may increase protein requirement (19). Ginn and co-workers (16) described the effect of surgery on the nutritional status of a 17-year-old male patient who had been dialyzed 2-4 times weekly for 3½ months. He was participating in a 32-day study to investigate the effect of quantity and quality of protein intake on nitrogen balance. Prior to the study, this adolescent patient was consuming 40 g of protein, of which 0.45 g/kg body weight was of high biological value. During the first 14 days of the nitrogen balance study he consumed 1.11 g of protein of high biologic value/kg body weight/day. Nitrogen balance was found to be slightly positive, peripheral neuropathy disappeared, serum albumin levels rose from 3.4 to 4.0 g/100 ml, and pre-dialysis levels for blood urea nitrogen rose from 54 to 90 mg/100 ml. A bilateral nephrectomy was performed on the 15th day, with glucose given intravenously for 3 days post-operatively. The diet was gradually increased to 0.75 g of high biologic protein/kg body weight. During the 14-day period following surgery, negative nitrogen balance persisted, serum albumin decreased to 3.8 g/100 ml, and blood urea nitrogen levels increased to above 120 mg/100 ml. Subsequently, a positive nitrogen balance was observed, and serum albumin rose to 4.2 g/100 ml. After 42 days, serum levels of total amino nitrogen and the essential amino acids remained within normal range, and pre-dialysis levels for blood urea nitrogen declined to a mean of 51 mg/100 ml. From the results of this study, Ginn and co-workers concluded that a diet containing

0.75 g of high biologic protein/kg body weight is necessary to maintain a slightly positive nitrogen balance, and to maintain normal levels of serum albumin.

The effect of drugs

The administration of drugs to combat infection also affects protein status. David and co-workers (19) reported that increased intakes of protein may be required by patients who are being treated with broad spectra antibiotics. These drugs kill colonic bacteria, thereby decreasing the amount of hydrolysis of urea in the colon. Consequently, synthesis of non-essential amino acids from endogenous urea is reduced.

The Value of Nitrogen Supplementation

The dietary implications of replacing amino nitrogen lost via hemodialysis have been discussed. Rubini and Gordon (20) felt that diet could supply enough nitrogen to compensate for the 4.8 g of protein and essential amino acids lost in effluent dialysate. Young and Parsons (21) also recommended adequate dietary protein, accompanied by sufficient energy to minimize the use of protein for energy. They felt that the addition of selected amino acids or protein hydrolysates to the dialysate bath was an expensive way to compensate for nitrogen losses.

Aviram and co-workers (23) suggested that diets containing 0.6-0.7 g of protein/kg body weight/day should compensate for even large losses of amino acids. Ginn et al. (16) recommended a daily intake of high biological value protein of approximately 0.75 g/kg body weight. They found that this amount was needed to maintain

equilibrium or a slightly positive nitrogen balance as well as a normal concentration of serum albumin in anephric patients dialyzed twice weekly. Comty (7) has suggested an even higher intake in order to achieve nitrogen retention. She stated that daily protein intake should not be less than 1 g/kg ideal body weight plus 3 g of additional protein to replace amino acids lost during dialysis.

IRON STATUS AND THE NEED FOR IRON IN MHD PATIENTS

Introduction

The role of the kidney in the regulation of erythropoiesis and its relationship to renal anemia has only been investigated within the past decade, although anemia has been linked with renal disease since 1835 (29). Anemia is one of the most common manifestations of chronic renal disease and invariably occurs (30-32). In early renal failure, anemia may be mild, becoming more severe as the disease progresses. The severity of the anemia correlates poorly with the degree of uremia; in some patients, the anemia remains fairly constant, in others, it rapidly progresses (33). Generally, the anemia stabilizes at hematocrit values ranging between 15-30% (29).

Characteristics of Renal Anemia

Morphological characteristics

Blood: Erythrocytes in peripheral blood samples are usually normocytic, normochromic (29, 32, 34). Hypochromia is uncommon unless blood loss has occurred, thereby creating a deficiency in the total content of body iron (31, 33, 35). Occasionally, erythrocytes appear macrocytic with some "burr cells" observed (29, 32, 34).

Bone marrow: Aspirates of marrow cells appear morphologically normal (33, 36, 37). Although normal or an increased number of reticulocytes is observed, the number is less than would be expected for the degree of anemia (29, 31—33). Marrow has been reported to be saturated with iron in both non-transfused patients and in those who have previously received blood transfusions (36).

Clinical characteristics

Clinical symptoms usually described by persons who have iron deficiency anemia include: general weakness, fatigibility, dyspnea on exertion and headache. Reduction of the level of hemoglobin brings a proportional increase in the incidence of the clinical signs of pallor of the skin, mucous membranes and nails. Fingernails may also be thin, brittle and display longitudinal ridging. Instead of being convex nails will occasionally appear concave or spoon-shaped (38). When hematocrit levels drop below 25% uremic patients become tired and breathless (39).

Iron Status of MHD Patients

Iron intake

The 1974 dietary allowance recommended for men is 10 mg/day (15). A "balanced average American diet" supplies approximately 6 mg of iron per 1000 kcal (40). Protein and potassium-containing foods may be restricted in hemodialysis patients and therefore, intake of iron, B-complex vitamins, calcium and ascorbic acid may also be reduced (41).

In 1966, Pendras and Erickson (42) outlined the results of a 7-day record of the food consumed by 5 hemodialysis patients. Most of the patients ate more than the prescribed diet which specified 40 g of protein and 400 mg of sodium. The mean dietary intake of iron was approximately 12 mg. In general, diets of patients ingesting more than 40 g of protein met the recommended level of iron. In 1968, Comty et al. (43) reported the results of research conducted to study the dietary requirement for iron, and to determine whether routine blood transfusions could be withdrawn from patients who had previously

received multiple transfusions. During a 3 year period, 15 subjects consumed a 60 g protein diet which was calculated to contain 9-11 mg of iron. A mean of 3.6 units of blood per month was required during the third year to maintain hematocrit levels of 22% or above. Mean serum iron of 139 mg/100 ml was within the normal range, and mean serum transferrin saturation of 57% was in the upper-normal range. Theoretical iron balance was a positive 6.2 g, and was estimated by subtracting the 900 ml monthly blood loss and menstrual loss from iron supplied via blood transfusion. The following year a "higher calorie diet containing a greater proportion of high biologic value protein", and a calculated iron content of 12-16 mg was consumed. The 15 patients were able to maintain parameters within normal ranges, as indicated by mean serum iron levels of 80 mg/100 ml and a serum transferrin percent saturation of 28%. A mean of 0.46 units of blood was transfused monthly to maintain hematocrit levels above 15%. Serum iron and transferrin per cent saturation were maintained within normal range for a year, inspite of decreased amounts of blood from transfusions, and illustrates the beneficial effect of diets containing increased quantities of iron, high biologic value protein, and energy.

Iron absorption

Intestinal absorption influences the supply of iron to the body. Approximately 10% of dietary iron is absorbed by healthy adult males, and this increases by a factor of 2 or 3 in iron deficient individuals with normally functioning kidneys (15). Comty et al. (43) found that 10 hemodialysis patients absorbed a mean of 51.0% of an

administered dose of $^{59}FeCl_3$ (range 44-88%), whereas 2 uremic patients not requiring dialysis absorbed 8.0% (range 3-13%) and 2 healthy controls absorbed 16.5% (range 13-20%). Similar results were reported in hemodialysis patients by Eschbach et al. (44), using a double isotope technique. They found a mean absorption of 58% in 16 subjects who had a mean transferrin saturation of 12% and therefore were considered iron deficient; a mean absorption of 3.5% in 8 subjects who had a mean transferrin saturation of 30% and were considered to be in normal iron balance; and a mean absorption of 3.6% in 10 subjects who had a mean transferrin saturation of 82% and were considered to have increased iron stores. In a 1974 review article, Koch et al. (45) reported the results of a study originally published in German which claimed to confirm the findings of Eschbach and co-workers (44).

Several workers have used a whole body counting technique. Koch et al. (45) found that hemodialysis patients with iron depleted stores absorbed iron at levels comparable to iron-depleted patients with normally functioning kidneys (45). They concluded that iron absorption is dependent on iron stores in the marrow. Brozovich et al. (46) found retention of ^{59} Fe, after 14 days, to be 31.2% in 7 patients reported as being iron deficient, whereas, 6 patients described as being "anemic but not iron deficient" retained 11.3%. Lawson and co-workers (47) measured whole-body radioactivity 20 days after the administration of oral ^{59} Fe. Mean absorption of iron was 2% in 10 patients consuming a 40 g protein diet which was not supplemented with oral iron. Lawson and co-workers concluded that "absorption did not appear to be related to the patients' iron stores, being distinctly lower than normal in both those with iron overload and in

two patients with iron deficiency." Unfortunately, the authors did not comment on the iron status of their patients, nor on the iron content of the diet consumed.

Iron utilization

The normal individual utilizes approximately 80% of intravenous radioiron for hemoglobin formation, but decreased utilization may be observed in patients with abnormal erythropoiesis (48). Eschbach and co-workers (37) gave radioiron intravenously to 13 hemodialysis patients of unspecified iron status. They utilized a mean of 55% of the radioiron (range 16-100%). Mean red cell utilization of 83% (range 67-96%) was determined in 3 of 4 patients of unspecified iron status who were studied by Carter et al. (49). Lawson and co-workers (47) administered iron intravenously to 10 male and 5 female patients and observed a mean incorporation of 24% (range 9-59%) into erythrocytes. Lawson et al. suggested that differences in the duration of dialysis, the dialytic process used, or the amount of hemolysis as possible reasons for the differences between their results and those reported by Eschbach et al. (37) and Carter et al. (49).

Utilization of orally ingested iron for hemoglobin synthesis was found by Brozovich and co-workers (46) to be greater than 45% in 12 of 13 patients (range 45-79%). One iron-laden patient utilized 19% of the radioiron dose, whereas 66-78% was utilized by individuals who were described as being iron deficient. Unlike Carter et al. (49), Brozovich et al. felt that hemodialysis patients effectively utilize both orally and parenterally administered iron.

Iron Loss

Non-dialyzed men

Iron loss, if it exceeds dietary intake and absorption, produces a negative iron balance. Healthy male adults lose approximately 1 mg of iron daily (40) via the gastrointestinal tract, skin and urine (50).

Dialyzed men

Men undergoing hemodialysis experience blood losses due to the dialytic treatment. These losses are in addition to the daily losses which occur in healthy adult men. Blood losses of 5-20 ml per dialysis have been reported as being common in hemodialysis patients (46), and this can represent an elemental iron loss of 5-20 mg per dialysis (11, 44). Assuming 12 dialyses per month, an iron loss of 60-240 mg can occur. Comty et al. (43) calculated a theoretical iron balance and found that a negative iron balance occurred, irrespective of dietary iron intake, when the monthly blood loss exceeded 250 ml. If the monthly iron loss was reduced to 125 mg, dietary intake, rate of absorption, loss through the skin, and faeces, and uptake from the dialyzer became important factors in determining iron balance.

There appears to be no information in the literature regarding the usual loss or gain of iron via the Gambro hemodialyzer, however, Lawson and co-workers (47, 51) have investigated the loss and gain of iron occurring in the twin-coil hemodialyzer. Although they experienced some technical difficulties, these authors concluded that the amount of iron gained is directly dependent upon the iron content of the water supply. The amount of iron lost into effluent

dialysate is small.

Erythrocyte Hemolysis

Increased hemolysis occurs in maintenance hemodialysis patients, thus reducing erythrocyte lifespan. Eschbach et al. (37) reported a mean erythrocyte half-life of 33 days (range 14-60 days), as compared to the normal half-life of 60 days. They also observed that increased duration of hemodialysis failed to improve erythrocyte lifespan in 5 patients studied for 10-35 months. Although the dialytic process may cause mechanical injury to the erythrocytes, the degree of uremia is of greater importance in determining the amount of hemolysis (29). The increased hemolysis, observed intravascularly in uremic patients, has been attributed by some workers to an unknown factor in the blood rather than to defective erythrocytes per se (31, 32, 34, 45). However, Yawata and co-workers (52) recently stated that uremic blood cells in some patients are actually defective and therefore prone to premature destruction. Using in vitro and in vivo methods, these authors showed that erythrocytes in affected patients have a decreased activity of the hexose monophosphate shunt pathway and thus the cells undergo premature destruction. Furthermore, they observed a red cell survival rate one-third of normal in 1 "severely affected patient" when the dialyzing fluid contained tap water. The survival rate became "completely normal" when the same patient was dialyzed for 12 weeks using de-ionized water, rather than tap water. Chloramine (NH_2Cl), the additive used to chlorinate tap water, was found to "potentiate" the tendency of uremic red cells to hemolyze prematurely. Use of chloramine-free water for the dilution of dialyzing concentrate

was recommended.

Renal Erythropoietin Factor (REF) Production

Anemia of chronic renal failure is primarily due to failure of the damaged kidney to produce REF, therefore, the conversion of a plasma globulin into biologically active erythropoietin is partially or completely abolished (30-32, 34, 35). Because erythropoietin regulates erythropoiesis, reduced blood levels of this substance results in decreased stimulation of the bone marrow (29, 32, 34, 45).

Bone Marrow Activity

Uremic toxins have a depressing effect on the bone marrow, therefore, marrow response to the limited supply of erythropoietin may be reduced (29, 30, 45, 53). Bone marrow in maintenance hemodialysis patients is capable of producing a normal number of red blood cells, but is not capable of making the increased number of cells required to compensate for the severe degree of anemia (29, 31, 34, 37). The anemia is described, therefore, as being hypoproliferative in nature (29, 32, 37).

Iron Supplementation

Because iron deficiency complicates the picture of renal anemia in maintenance hemodialysis patients, several methods have been used to improve their iron status. Blood transfusions have been used, but are not a popular means of treating iron deficient patients because of the risks involved (36, 49). Iron given parenterally by-passes

the intestinal absorptive mechanism, thus excessive administration may result in hemosiderosis (54).

Others have given iron orally to treat the anemia. Strickland and co-workers (55) stated that iron administered orally is unlikely to cause chronic overload, and can be effective, although the effectiveness compared to parenteral iron is unknown. They conducted a double blind, cross-over study with 34 patients who consumed 100 mg per day of elemental iron, given as ferrous sulphate, during a 12 week treatment period. Mean and standard deviation of serum iron was 87.6 ± 18.6 ug/100 ml for the treatment period, compared with 66.8 ± 13.2 ug/100 ml during the control period, when a placebo was given. The difference was highly significant ($P < 0.01$). Results of trend analysis indicated that patients treated with oral iron showed significantly greater improvement ($P < 0.05$) in hemoglobin, hematocrit, mean corpuscular volume and red cell volume than patients treated with a placebo. Alth[illegible]e hemoglobin concentration at the end of a 12 week trea[illegible] was only 1.3 g/100 ml higher than at the end of place[illegible]ent, patients consuming the iron supplements reported being i[illegible]reathless. The authors felt that 100 mg of elemental iron gi[illegible] daily was sufficient to compensate for iron losses during dialysis[illegible]5). Brozovich et al. prescribed 600 mg of ferrous sulphate daily f[illegible]3 months to 1 female and 2 male patients who had decreased marrow [illegible]ores and were therefore considered to be iron deficient; and to 3 male patients who had normal stores of iron in the marrow. Whereas the latter group maintained their iron stores, the iron deficient group failed to replenish their stores following treatment. These authors recommended "prolonged oral iron therapy" (46). Crim

and Calloway (56) proposed a nutrition program which could be used for adult patients on hemodialysis. The mineral supplement contained 5 mg of elemental iron per 800 kcal (or 6.25 mg/1000 kcal). They felt that this level of iron was sufficient to provide for the usual fecal and dermal losses encountered in patients undergoing hemodialysis.

EXPERIMENTAL PROCEDURE

OBJECT

To study the effect on energy, protein and iron status of superimposing a broad spectra nutritional supplement on the daily diets of uremic patients undergoing maintenance hemodialysis.

SUBJECTS

Twenty-four patients judged medically stable and reliable were informed of the study, and asked if they wished to participate. Although 16 agreed, only 5 patients volunteered to consume 1 can of MJ 7014 and the supplementary vitamin pills daily. The remaining 11 patients conditionally agreed to participate; they wished to consume only the vitamin pills. Unknown to the patients placebo pills, identical to the vitamins taken by the experimental group, were given to the control group. Two groups were formed: the control group (11 subjects) and the experimental group (5 subjects). Two female subjects in the control group and 1 female subject in the experimental group were unable to complete the study due to renal transplantation and major surgery, respectively. As energy, protein, and iron requirements of women differ from men, information collected from 2 remaining female subjects in the control group has been excluded. Data is presented for the 7 and 4 male subjects who served as the control and experimental groups respectively (Table I).

At the beginning of the study, all subjects had been on maintenance hemodialysis longer than 6 months, and were either hospital out-patients or on home dialysis. With the exception of

TABLE I

Description of subjects.

Subject	Sex	Marital Status	Age	Height	Initial Weight	Kidney Disease[1]
Control Group			years	cm	kg	
1	Male	Single	22	172	50.8	Familial nephritis
2	Male	Single	38	146	51.4	Fanconi syndrome
3	Male	Single	34	197	76.6	Chronic glomerulonephritis
4	Male	Married	29	172	60.2	Chronic glomerulonephritis
5	Male	Married	47	174	69.2	Chronic glomerulonephritis
6	Male	Married	60	167	52.0	Chronic glomerulonephritis
7	Male	Single	28	169	67.8	Essential hypertension[2]
Mean ± SD[3]			37±13	171±15	61.1±10.3	
Experimental Group						
8	Male	Married	53	167	63.5	Chronic glomerulonephritis
9	Male	Single	29	173	69.0	Chronic glomerulonephritis
10	Male	Married	46	179	82.2	Chronic glomerulonephritis
11	Male	Married	57	182	89.1	Polycystic kidney disease
Mean ± SD[3]			45±11	175±7	76.0±11.8	

[1] The underlying kidney disease responsible for the uremic state.
[2] Subject 7 was anephric; the remaining subjects were bi-nephric.
[3] Mean ± standard deviation of the mean.

subject 7, each was dialyzed 3 to 8 hours thrice weekly. A glucose-free dialyzing fluid was used by all subjects. Eight months previous to, and during the study, de-ionized water was used to dilute the dialyzing concentrate. Table II describes the hemodialysis data.

STUDY PERIOD

The study was conducted during summer and autumn, with the first subjects beginning in mid-June 1973. Each subject participated for 20 weeks. Details of the schedule are outlined in Appendix Table 1.

OBJECTIVE METHODS USED FOR THE EVALUATION OF NUTRITIONAL STATUS

Dietary Intake

Food

The 11 subjects were encouraged to eat the same food they usually ate and to follow the same habits established prior to the study. They were also asked to continue their usual pre-study physical activities; no attempt was made to influence or change either the energy intake or expenditure of the subjects.

A 7-day intake record was used to assess usual daily food intake, as food consumption and eating habits of maintenance hemodialysis patients had been observed to vary between week-days and week-ends, and between days of hemodialysis and days when hemodialysis was not required. Three 7-day intake records were kept by each subject. The control group recorded their food consumption during weeks 2, 8-9 and 20, whereas the experimental group recorded their

TABLE II

Hemodialysis history, A-V shunt, and routine followed throughout the study.

Subject	Time[1]	A-V. Shunt[2]	Place[3]	Dialyzer[4]	Frequency[5]	Duration[6]
Control Group						
1	52	Cannula	Hospital	Gambro	3	5
2	8	Fistula	Hospital	Gambro	3	7
3	63	Fistula	Hospital	Gambro	3	8
4	16	Cannula	Home	Standard Kiil	3	8
5	7	Cannula	Hospital	Gambro	3	6
6	24	Cannula	Hospital	Gambro	3	6
7	45	Fistula	Hospital	Gambro	2	12
Experimental Group						
8	28	Fistula	Hospital	Gambro	3	8
9	80	Cannula	Home	Standard Kiil	3	8
10	56	Cannula	Home	Standard Kiil	3	8
11	16	Fistula	Hospital	Gambro Gambro	3	8

[1]Length of time on maintenance hemodialysis program, expressed in months, as of mid-June 1973.
[2]Arterio-venous shunt used to attach the blood lines of the subject to the dialyzer.
[3]Place of hemodialysis.
[4]Machine used during the study. All Gambro machines used were the 17 micron model.
[5]Frequency of hemodialysis per week.
[6]Duration of each dialysis, expressed in hours.

consumption during the pre-study period, and then during weeks 5-7 and week 20. The experimental group was also asked to record the amount, time and the way in which the MJ 7014 was consumed. Appendix Table 2 outlines the format used for the intake record.

Each food item recorded by the subjects was coded according to Composition of Foods. Handbook No. 8 (57), and the nutrient composition calculated by computer. The 7-day totals and respective mean intake per day were computed for energy, protein, and iron for each of the 3 food record periods.

Nutritional supplement (MJ 7014)

The nutritional supplement used was Product 7014, an experimental renal diet produced and supplied by Mead Johnson Canada. This product was selected because it provided a source of energy; contained essential amino acids as the major source of nitrogen; had a broad spectra of vitamins and minerals; yet was restricted in sodium and potassium content. See Table III for the nutritional composition, and Table IV for a list of the ingredients of MJ 7014.

To test for acceptability samples of both the imitation orange and strawberry flavored powders were diluted with water according to directions and taste-tested by hemodialysis patients and staff. Although subjectively described as "sweet", both flavors of MJ 7014 were acceptable. To encourage consumption of the supplement, recipes and suggestions of how MJ 7014 might be incorporated into other foods were given to each patient (Appendix Table 3).

In addition to their usual food intake, the experimental group consumed MJ 7014 ad libitum. Each subject was encouraged to

TABLE III

Nutritional composition of the supplement (MJ 7014)[1].

Energy	1600 kcal	Fat soluble vitamins	
Per cent of calories		Vitamin A	5000 IU
Protein	5.3	Vitamin D	400 IU
Fat	2.8	Vitamin E	30 IU
Carbohydrate	91.9		
		Water soluble vitamins	
Total Protein	21.0 g		
		Thiamine	1.4 mg
Elemental amino acids:		Riboflavin	1.7 mg
L-isoleucine	1.4 g	Niacin	18.0 mg
L-leucine	2.2 g	Pyridoxine	2.0 mg
L-lysine	1.6 g	Pantothenic acid	10.0 mg
L-threonine	1.0 g	Folic acid	0.1 mg
L-tryptophan	0.5 g	Vitamin B_{12}	5.0 mcg
L-valine	1.6 g	Ascorbic acid	60.0 mg
L-methionine + L-cystine	2.2 g	Choline	85.0 mg
L-phenylalanine + L-tyrosine	2.2 g	Minerals	
L-histidine	1.0 g		
		Iron	12.0 mg
Fat	4.8 g	Copper	1.5 mg
		Zinc	8.0 mg
Carbohydrate	368.0 g	Manganese	2.0 mg
		Iodine	140.0 mcg
Electrolytes			
Sodium	185.0 mg		
Potassium	310.0 mg		
Calcium	520.0 mg		
Magnesium	100.0 mg		
Phosphorus	180.0 mg		
Chloride	400.0 mg		
Sulphur	550.0 mg		

[1]The amount of nutrients contained in 1 can or 403.6 g of MJ 7014

TABLE IV

Ingredients contained in the nutritional supplement (MJ 7014)[1].

Corn syrup solids, granulated sugar, whey protein concentrate, egg white solids, corn oil, malic acid, calcium carbonate, L-histidine monohydrochloride monohydrate, L-methionine, citric acid, fumaric acid, L-phenylalanine, L-leucine, L-lysine monohydrochloride, L-valine, magnesium phosphate dibasic, L-isoleucine, artificial flavor, choline bitartarate, L-threonine, L-tryptophan, potassium citrate, polysorbate 60, artificial color, ascorbic acid, sodium citrate, glutathione, dried ferrous sulphate, zinc sulphate, d-α-tocopheryl acid succinate, niacinamide, calcium pantothenate, vitamin A & D powder, manganese sulphate, cupric sulphate, pyridoxine HCl, riboflavin, thiamine mononitrate, potassium iodide, folic acid, vitamin B_{12}.

[1] The ingredients contained in 1 can or 403.6 g of MJ 7014.

consume 1 can of MJ 7014 per day which could supply 1600 kcal and 21 g of protein of high biologic value (Table III). The liquid used to dilute the powder was included as part of the daily fluid allowance of each subject. To prevent and/or reduce the loss of nutrients during hemodialysis (11, 58), subjects were asked to consume most of the MJ 7014 after the completion of hemodialysis, or several hours prior to hemodialysis.

Vitamin supplements

Maintenance hemodialysis patients usually have a greater need for supplementary vitamins than does the normal individual (11, 58, 59). They may consume limited amounts of food from some food groups. Food may be prepared to deliberately reduce the sodium and potassium content but other water soluble nutrients may also be leached from the food (7). Vitamins are also lost during hemodialysis treatment. Thiamine, riboflavin, niacin, pyridoxine, pantothenic acid, folic acid, and ascorbic acid are of particular concern. Both the experimental and control groups were given supplements to be taken post-dialysis, previous to or following a meal. The control group, however, were given placebos which were indistinguishable from the capsules and tablets given the experimental group (Table V). Ascorbic acid has been reported to shorten the prothrombin time of animals receiving coumarin anticoagulant drugs (60, 61), therefore the subjects were asked to consume the vitamin capsule and anti-coagulant drugs several hours apart.

In addition to the supplementary pills, both groups also took any medications prescribed prior to, or during the study. These

TABLE V

Nutritional composition of the vitamin capsule and folic acid tablet[1] consumed daily by the experimental group.

Capsule	Content
Thiamine mononitrate	30 mg
Riboflavin	15 mg
Niacinamide	50 mg
Pyridoxine HCl	5 mg
Calcium pantothenate	20 mg
Ascorbic acid	400 mg
Tablet	
Folic acid	5 mg

[1]The B + C 400 multi-vitamin capsule and folic acid tablet were prepared and provided gratis for the study by Mead Johnson Canada, Toronto, Canada.

included: vitamin preparations, calcium-containing compounds, phosphate and potassium-binding agents, and dihydroxytachysterol (Tables VI, VII).

Anthropometric Evaluation

Height and weight

At the beginning of the study, the subjects were asked their height, which was recorded. The attending nephrologists evaluated the state of hydration of each subject and judged the post-dialysis weights of week 1 to be "ideal dry weight". Each subject was weighed using the same balance during weeks 1, 9, 13 and 20. To reduce the influence of the state of hydration weight was recorded immediately post-dialysis.

Mid-arm circumference

The mid-arm circumference was determined on the dominant side of the body with the subjects standing erect but relaxed (62-65). Anatomically, the site was located mid-point between the acromion of the scapula and the olecranon, as described by the Committee on Nutritional Anthropometry, Food and Nutrition Board, National Research Council (64). A fiberglass tape measure was held firmly, and encircled the arm without indenting the skin. One reading was taken per measurement, with all values rounded to the nearest 0.5 cm. Measurements were done, post-dialysis, during weeks 1, 7, 13 and 20.

Skinfold calibration

Lange skinfold calipers, which exerted a standard jaw pressure of 10 g/mm^2, were used to determine the skinfold thickness

TABLE VI

Additional vitamins[1] consumed daily by the experimental group.

Subject	Vitamin preparation	Daily Dosage	Daily Frequency
8	Folic acid	5 mg	once
	Vitamin capsules[2]	2	once
9	Folic acid	5 mg	once
10	None taken	-	--
11	Folic acid	5 mg	twice

[1] Pre-study vitamins which were consumed in addition to those provided during the study.
[2] Composition unknown.

TABLE VII

Composition of the vitamin preparations consumed during the study by the control group.

Subject	Vitamin preparation	Daily Dosage	Daily Frequency
1	Multicebrin[1]	1 capsule	once
2	None taken	-	-
3	Multicebrin[1]	1 capsule	once
4	Multicebrin[1]	1 capsule	once
5	None taken	-	-
6	Folic acid	5 mg.	twice
7	None taken	-	-

[1]Multicebrin is produced by the Eli Lilly Company. One capsule contains: vitamin A, 10,000 IU; vitamin D, 400 IU; vitamin E, 10 IU; thiamine, 3 mg; riboflavin, 3 mg; niacinamide, 25 mg; vitamin B_6, 1.5 mg; pantothenic acid or derivative, 5 mg; vitamin B_{12}, 3 mcg; and ascorbic acid, 75 mg.

of the triceps and sub-scapula. All calibrations were performed on the dominant side of the body, with the subject standing erect though relaxed (62-65). Triceps skinfold thickness was determined at the anatomical site located mid-way between the lateral margin of the acromial process of the scapula, and the tip of the olecranon. A vertical crease was formed parallel to the long axis of the arm; a double thickness of skin plus sub-cutaneous fat was then grasped, with the calipers applied 1 cm below the left thumb and the index finger (66). Sub-scapula calibration was conducted at the anatomical site located immediately below the tip of the scapula bone. Extending medially upward and laterally downward, a crest was formed at a 45° angle to the backbone. A double thickness of skin plus sub-cutaneous fat was grasped with the left thumb and index finger, and the calipers applied 1 cm away from the fingers in the laterally downward position (66). One triceps reading was taken, then one sub-scapula reading. Alternate readings were done until a total of 3 readings were obtained for each site. Readings were recorded to the nearest 0.5 mm and a mean determined. Measurements were calibrated, post-dialysis, during weeks 1, 7, 13 and 20.

Per cent body fat

Body density was calculated from values obtained for triceps and sub-scapula skinfold thickness, using the miltiple regression equation described by Sloan and Shapiro (67): Density = 1.0950 - 0.0015 (triceps skinfold thickness) - 0.0012 (sub-scapula skinfold thickness). Per cent body fat was then calculated, as described by Wilmore and Behnke (62): % Body fat $= \left[\frac{4.570}{\text{Density}} - 4.142\right] \times 100$. A computer was used to calculate all values.

Cross-sectional fat area

Cross-sectional fat area is equal to arm area minus muscle area, and was determined by nomogram (68).

Lean body weight

Lean body weight was calculated by computer, using the formula described by Wilmore and Behnke (62): Lean body weight = post-dialysis weight - (post-dialysis weight x % body fat).

Arm-muscle circumference

Arm-muscle circumference was determined by nomogram, from triceps skinfold thickness and arm circumference values (68).

Biochemical Evaluation

Serum urea nitrogen, albumin and transferrin were determined to assess protein-calorie status; and hemoglobin, hematocrit, serum iron, total iron binding capacity and serum transferrin per cent saturation to assess iron status. Blood samples were collected from the arterial shunt during weeks 1, 8, 12 and 20. Four samples were taken each time: 1-15 ml sample for pre-dialysis hemoglobin, and hematocrit assessment; 1-15 ml sample for pre-dialysis serum transferrin, serum iron, and total iron binding capacity assessment; 1-15 ml sample for the pre-dialysis determination and 1-15 ml sample for the post-dialysis determination of serum urea nitrogen, and albumin. All biochemical determinations were done in the centralized laboratory of the University of Alberta Hospital. Serum transferrin was determined by the radial diffusion method of Mancini et al. (69). All other biochemical values were determined by routine methods and automated equipment.

Blood transfusions and extraordinary blood loss due to ruptured hemodialyzer membranes or hemorrhaging represent a gain or loss of iron to the body and could affect biochemical findings, thus, gains or losses of blood were recorded as they occurred. Iron dextran was injected parenterally throughout the study, as individually required.

Hair Morphology Evaluation

Bradfield and co-workers (70) reported that alterations in hair root morphology and diameter could be used to evaluate protein-calorie status. The semi-quantitative method described by them was employed to classify the roots of hair and to determine the diameter of the root. Samples were collected during weeks 1, 7, 13 and 20. To reduce any possible influence of the state of hydration, all hair samples were collected post-dialysis.

From 2-3 sites in the occipital area of the head, a total of approximately 50 hairs were epilated by quick, forceful pulls. Small curved mosquito forceps, one prong snuggly fitted with a tygon tip, were employed. Using a 60 x magnification and a 10 mm ocular micrometer divided into 100 parts, each root was microscopically classified according to its morphology (70, 71). Fiften anagen hairs were randomly selected and the root diameters were measured in triplicate. A mean diameter was determined for each sample (70, 71).

SUBJECTIVE METHODS USED FOR THE EVALUATION OF NUTRITIONAL STATUS

Diet and Medical History Questionnaire

A questionnaire designed to obtain subjective data concerning

the dietary and medical background of the subjects was administered during weeks 5 and 6. Personal opinions and experiences regarding kidney disease, hemodialysis, and therapeutic nutrition practices were elicited (Appendix Table 4).

Subject-Researcher Discussions

Throughout the study, all subjects were frequently contacted to deepen subject-researcher rapport, to encourage continued consumption of the supplements or placebos, and to obtain subjective responses to all aspects of the study. Subjects who were out-patients were seen while being hemodialyzed at the hospital; subjects on home dialysis were visited in their homes, or contacted by telephone.

Feedback Questionnaire

At the completion of the study, all subjects were interviewed to obtain their opinions regarding the experience. Of particular concern were the reaction of the subjects to the nutritional supplements or placebos, and to the methods used to obtain objective data (Appendix Table 5).

STATISTICAL METHODS USED TO EVALUATE NUTRITIONAL STATUS

A computer was used for all calculations. For each parameter, mathematical computation included mean and standard deviation. Unpaired 2-tailed 't' tests were used to determine significant differences between the control and experimental groups; paired 2-tailed 't' tests were used to determine significant differences within groups.

RESULTS AND DISCUSSION

CONSUMPTION OF THE NUTRITIONAL SUPPLEMENT MJ 7014

All 4 members of the experimental group began consuming MJ 7014 during week 1 of the study, and continued for at least 11 weeks. Only 1 subject consumed MJ 7014 for 20 weeks. During the latter part of the study, the other 3 subjects were hospitalized for treatment of infection and/or surgery and discontinued consumption of the supplement. Thus MJ 7014 was consumed by all subjects in the experimental group for a mean of 15 weeks (range 11-20). Although 1 can of MJ 7014 was initially taken per day, 1/3-3/4 of a can was the quantity most frequently consumed by the experimental group (Appendix Table 6).

ENERGY STATUS

Energy Intake

Energy intake from diet was consistently maintained at approximately 2100 kcal and 2400 kcal by the control and experimental groups, respectively (Table VIII). Total energy intake of the experimental group was significantly greater than the control group, during weeks 7-8 (Table VIII). Total intake of energy by the experimental group was significantly greater ($P < 0.05$) than their dietary intake during weeks 7-8, and may be attributed to the consumption of MJ 7014.

Males, 23 to 50 years of age, who are 172 cm tall, weigh 70 kg, and whose activity level may be described as "light" require approximately 2700 kcal, or 39 kcal/kg daily (15). The control group

TABLE VIII

The effect of nutritional supplementation on energy status of maintenance hemodialysis patients.

	n	Week 1	7-8	12-13	20
Control group					
Total energy intake (kcal)	5	2160 ± 466[1]	2190 ± 423[g]	---	2070 ± 474
Post-dialysis weight (kg)	7	61.1 ± 10.3	62.0 ± 10.7	61.7 ± 10.0[i]	62.3 ± 10.4[j]
Total energy intake/kg body weight (kcal)	7	36 ± 11	39 ± 11	---	36 ± 11
Dietary energy intake/kg body weight (kcal)	7	36 ± 11	39 ± 11	---	36 ± 11
Body fat (%)	7	13 ± 3	13 ± 3	12 ± 3	12 ± 3
Triceps skinfold (mm)	7	9 ± 3	8 ± 3	8 ± 3[a]	9 ± 3[a]
Sub-scapula skinfold (mm)	7	9 ± 4[m]	10 ± 4	9 ± 4	9 ± 3
Sum of skinfolds (mm)	7	18 ± 6	18 ± 6	16 ± 6	17 ± 6
Cross-sectional fat area (cm^2)	7	9 ± 2	9 ± 4[bc]	8 ± 4[cd]	10 ± 3[bd]
Telogen hair (%)	7	18 ± 10	19 ± 12[e]	27 ± 14[e]	16 ± 11
Experimental group					
Total energy intake (kcal)	4	2740 ± 855	3310 ± 501[gh]	---	2540 ± 789
Dietary energy intake (kcal)	4	2490 ± 820	2370 ± 556[h]	---	2410 ± 805
Post-dialysis weight (kg)	4	76.0 ± 11.8	76.8 ± 12.3	78.5 ± 10.2[i]	78.6 ± 11.8[j]
Total energy intake/kg body weight (kcal)	4	36 ± 11	44 ± 9	---	33 ± 13
Dietary energy intake/kg body weight (kcal)	4	33 ± 13	32 ± 10	---	32 ± 14
Body fat (%)	3	18 ± 6[k]	15 ± 9	15 ± 6[k]	16 ± 6
Triceps skinfold (mm)	3	12 ± 4[l]	10 ± 5	10 ± 5[l]	9 ± 5
Subscapula skinfold (mm)	3	17 ± 7[mn]	15 ± 9	14 ± 7[n]	15 ± 8
Sum of skinfolds (mm)	3	29 ± 11[op]	25 ± 13	24 ± 12[o]	25 ± 12[p]
Cross-sectional fat area (cm^2)	3	14 ± 5	13 ± 7	13 ± 7	12 ± 7
Telogen hair (%)	3	29 ± 12[q]	16 ± 9[q]	26 ± 10[r]	6 ± 5[r]

[1] Values are mean ± standard deviation of mean.
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

had a mean age of 37 years, height of 171 cm (Table I), and post-dialysis weight ranging from 61-62 kg (Table VIII). Collectively, the activity level of the 7 control subjects might be described as "light". Although age, height and activity level of the control group was similar to the 1974 RDA reference man, they consumed 36-39 kcal/kg daily (Table VIII), and weighed about 8-10 kg less. The experimental group had a mean age of 45 years, height of 175 cm (Table I), and post-dialysis weight ranging from 76-79 kg (Table VIII). Collectively, their activity level could be described as "light". Therefore, the experimental group were older, taller, and heavier than the control group, although activity levels were comparable. Age and estimated activity level of the experimental group was similar to the 1974 RDA reference man, but height and weight was somewhat greater. During the study, the experimental group consumed a total energy intake ranging from 33-44 kcal/kg (Table VIII). Only when MJ 7014 was consumed by all subjects in the experimental group (weeks 7,8) did their energy intake per kg body weight exceed that of the control group and the amount suggested for the reference man described in the 1974 Recommended Dietary Allowances (15).

Kopple and co-workers (17) documented actual consumption of energy in 23 out-patients undergoing twice-weekly hemodialysis. Estimated energy intakes of 33 $\pm$ 4 kcal/kg and 39 $\pm$ 6 kcal/kg body weight were reported in patients prescribed 0.75 g of protein/kg and 1.25 g of protein/kg body weight, respectively (17). In the present study, total energy intake per kg body weight ranged between 36-39 kcal/kg in the control group, and between 33-44 kcal/kg in the experimental group (Table VIII). Hence, energy intake of both groups participating

in the present study was comparable to, or greater than those observed by Kopple et al. (17).

Pendras and Erickson (42) reported a mean intake of about 1750 kcal (range 1317-2363 kcal) in 5 patients who were prescribed a 40 g protein diet and dialyzed a total of 20-40 hours per week. Simmons et al. (6) reported the unpublished data of P. F. Gulyassy, P. Y. Schoenfield, and T. M. LeRose, who conducted a "well-controlled study of food intakes of 6 reliable adult patients on dialysis". Average intakes of 1420 kcal (range 1300-1825 kcal) or 67% of their calculated ideal intake (range 43-89%) were found (6). Total intake of energy consumed by the present control group was similar to levels of intake found in these 2 studies, whereas the energy intake of the experimental group was consistently greater.

Effect of Energy Intake on Parameters Assessing Nutritional Status

Post-dialysis weight

Post-dialysis weight of the control and experimental groups remained within narrow ranges of 61-62 kg, and 76-79 kg respectively (Table VIII), hence no significant differences were found within these 2 groups. Post-dialysis weight of the experimental group was significantly greater ($P < 0.05$) than the control group only during weeks 12-13 and 20.

Body weight is the simplest anthropometric measurement of growth and nutrition (72), and its accurate assessment is essential for the clinical management of hemodialysis patients (73). In studies of hemodialysis patients body weight has been reported to measure the success of nutritional rehabilitation; describe nutritional

status; indicate changes in body composition; and, to evaluate the efficacy of dietary treatment (8, 9, 14, 17, 42, 74).

Post-dialysis weight of the control group in this study was approximately 8-9 kg below the 70 kg cited for the reference man in the 1974 RDA (15), whereas weight of the experimental group was approximately 6-9 kg greater than the reference man. Jelliffe (66) calculated the percentage of standard weight for height of nude adult males of average frame size. Compared with the calculations of Jelliffe, the control group were found, through the study, to be 90-94% of the standard weight expected for adult males of 171 cm height. The experimental group were 105-109% of the standard weight expected for adult males of 175 cm height during weeks 1 through 13, and 110-114% of their standard weight during week 20.

Body fat

Water, fat, and body cell mass are the major components of body weight (75). The amount of fat in a body is an expression of caloric balance (76). Per cent body fat of the control group remained fairly constant at 12-13%, hence no significant differences were observed with time (Table VIII). Per cent body fat of the experimental group decreased significantly ($P < 0.05$) from 18% during week 1 to 15% during weeks 12-13, then gradually increased to 16% during week 20 (Table VIII). At the same time energy intake increased, although not significantly.

Using the formula of Brozek et al., Wilmore and Behnke (62) determined a mean body fat content of about 15 $\pm$ 5% in 133 healthy male adults, whose mean age, height, and weight were about 22 years,

177 cm, and 76 kg, respectively. Applying the same formula mean values of the control group were 2-3% lower than those found by Wilmore and Behnke, whereas, those of the experimental group were comparable. Hence, the control group had somewhat reduced fat stores, whereas fat stores in the experimental group were normal.

Comty (74) assessed body fat stores in 17 patients after 7-30 months of treatment with twice-weekly dialysis and a "strict diet . . . high in calories and restricted in protein, sodium, potassium, and water content". Following treatment, 65% achieved normal weight. However, in 80% of the subjects studied, this weight was not a reflection of increased lean body mass, but rather, a reflection of added body fat and/or fluid retention. Comty concluded that the "high" calorie diet, restricted in protein, was insufficient to restore normal body composition. Diets adequate in energy resulted in normal fat stores in the experimental group participating in the present study.

Body composition of 77 patients with renal failure was reported by Coles (28). Of this group, 29 hemodialysis patients were studied. Total body fat was calculated from measurement of skinfold thickness at 9 sites. Data was collected at the commencement of dialytic therapy and every 3 months thereafter, for 1 year. The hemodialysis patients received at least 50 g of protein per day, but energy level of the diet was not specified. At 6 months, 2.2 kg of body fat ($P < 0.01$) had been gained. At 9 months, mean body fat had decreased, due to marked loss of fat in 2 subjects with inter-current infections. One year after starting dialytic therapy, the proportion of body fat was within the range of 15-25%, defined by Coles as being normal. The control and experimental groups in the present study may

be described as having below normal and normal proportions of body fat, respectively, as defined by Coles.

Triceps skinfold thickness

Triceps skinfold thickness provides a simple, practical measure of sub-cutaneous fat, and thus is an indication of body energy reserves (66, 72). Skinfold thickness of the control group increased significantly ($P < 0.05$) between weeks 12-13 and 20, and decreased significantly ($P < 0.05$) in the experimental group between weeks 1 and 12-13 (Table VIII). These changes were not accompanied by significant differences in energy intake.

The United States Department of Health, Education and Welfare reported the results of anthropometric data gathered during the (U.S.A.) National Health Survey of 1960-62 (77). Using Lange skinfold calipers, triceps skinfold thickness was measured on 3,091 adult civilian men, whose ages ranged from 18-79 years. Mean triceps skinfold thickness was found to be 13 mm; with 90% of the values occurring between 5-28 mm. Mean thickness of triceps skinfold of the experimental and control groups were consistently below 13 mm, which would indicate reduced fat stores.

Sub-scapula skinfold thickness

Sub-scapula skinfold thickness is often used as a secondary site for adults (66). In the present study, values for the control group ranged between 9-10 mm, hence no significant differences were found with time (Table VIII). Like the triceps skinfold thickness, a significant decrease ($P < 0.05$) was observed in the sub-scapula skinfold thickness of the experimental group, between weeks 1 (17 mm) and weeks

12-13 (14 mm)(Table VIII).

Sub-scapula skinfold thickness was measured during the American health survey of 1960-62 (77). A mean value of 15 mm was found in 3,091 adult civilian men, with 90% of the values occurring between 7-30 mm. Mean thickness of the sub-scapula skinfold of the control group was consistently below 15 mm, whereas values of the experimental group were similar to those found in the American study. Both the experimental and control groups, however, maintained values within the 90% range described above. Thus, body fatness was normal in the experimental group, and somewhat reduced in the control group. These observations in the experimental group were not similar to those found using the triceps skinfold thickness.

Sum of skinfold thickness

The sum of triceps and sub-scapula skinfolds exhibits the combined distribution that would be expected on the basis of the component parts. In men, sub-scapular skinfold thickness contributes to the larger part of the combined sum (77). The sum in the control group ranged from 16-18 mm (Table VIII), with no significant differences observed. In the experimental group, however, sum of skinfold thickness was significantly greater ($P < 0.05$) in week 1 than in weeks 12-13 or week 20 (Table VIII). Energy intake, however, did not vary significantly in the experimental group between weeks 1 and 12-13, or between weeks 1 and 20.

A mean thickness of 28 mm was reported in 3,091 male civilian men by the United States Department of Health, Education and Welfare

(77), with 90% of values occurring between 12-54 mm. Like triceps and sub-scapular skinfold thickness, the sum of skinfold thickness of the control group was consistently lower than the previously mentioned mean values, but within the range of values found for 90% of the healthy American men. Body fatness of the control group may be described as being somewhat reduced. The sum of skinfold thickness for the experimental group was similar to the mean thickness of 28 mm reported for the average American male (77).

Cross-sectional fat area

The cross-sectional fat area of the arm is a fairly new tool which provides an age-independent assessment of body energy reserves (68). Throughout the study, cross-sectional fat area of the control group varied erratically throughout the study (Table VIII). These fluctuations were statistically significant but were not accompanied by similar changes in energy intake. Cross-sectional fat area of the experimental group did not vary significantly during the study (Table VIII).

A standard of 17.4 cm^2 was derived for the cross-sectional fat area of the arm of adult males by Gurney (78), using the standard arm measurements of Jelliffe (66). The consistently lower mean values of 8-10 cm^2 for the control group would indicate decreased body reserves of energy. Cross-sectional fat area of the arm ranged from 12-14 cm^2 in the experimental group, less than the 17.4 cm^2 standard suggested by Gurney (78). Body reserves of energy of the experimental group were thus judged to be somewhat low by this parameter.

Proportion of hair in the telogen phase

An increased proportion of hair in the telogen, or resting phase has been attributed to caloric deficiency by Crounse et al. (79). The proportion of hair in the telogen phase ranged between 16-27% in the control group, with a significantly greater ($P < 0.05$) proportion noted during weeks 12-13 than weeks 7-8 (Table VIII). The proportion in the experimental group ranged between 6-29%, with a significantly reduced ($P < 0.05$) proportion noted during weeks 7-8 than in week 1; and during week 20 than during weeks 12-13 (Table VIII).

Samples containing less than 20% of the hair in the telogen phase were considered "normal" by Bradfield, whereas samples containing 20-45% were considered indicative of "moderate protein-calorie malnutrition" (70). Strict application of these standards would suggest that the control group had a "normal" status of protein-calorie nutrition during weeks 1, 7-8 and 20, but suffered from moderate protein-calorie malnutrition during weeks 12-13. Similarly, the experimental group could be described as having a normal protein-calorie status during weeks 7-8 and 20, but suffering from moderate protein-calorie malnutrition during weeks 1 and 12-13. Results of dietary and other anthropometric parameters would indicate that protein-calorie malnutrition was absent in both groups. The standards which were established by Bradfield, were developed from studies with children having Asian and Negroid hair types, and were suggested as being useful for assessing preschool children (70). Because of differences in race and age, the Bradfield standard may not be strictly applicable to Caucasian adult men who require maintenance hemodialysis.

PROTEIN STATUS

Protein Intake

Total daily intake of protein ranged from 77-84 g in the control group, and from 89-103 g in the experimental group (Table IX). No significant differences were found within these group values. During week 20, total intake of protein by the experimental group was significantly greater ($P < 0.05$) than total intake of protein by the control group (Table IX). The dietary intake of protein by the experimental group was relatively constant, ranging from 86-91 g daily (Table IX). During week 20, the dietary intake of protein by the experimental group was also significantly greater ($P < 0.05$) than the intake of protein by the control group.

The control group consumed 1.3-1.5 g of protein/kg body weight, whereas the experimental group consumed 1.2-1.4 g (Table IX). The intake by the experimental group without the MJ 7014 was less than the amount consumed by the control group. Intakes ranged from 1.1-1.2 g of protein/kg body weight (Table IX). The Food and Nutrition Board, National Research Council (15) suggested that an intake of mixed protein of 0.8 g/kg body weight would be adequate to meet the daily protein needs of the majority of healthy males between 23-50 years (15). Hence, the daily intake of protein by both groups was approximately 1½ times the 1974 RDA.

The amount of protein consumed by both the control and experimental groups in this study was greater than amounts found by others. Kopple et al. (17) followed 2 groups of patients and found that they consumed from 0.8-1.2 g of protein/kg body weight. Pendras

TABLE IX

The effect of nutritional supplementation on protein status of maintenance hemodialysis patients.

	n	Week 1	7-8	12-13	20
Control group					
Total protein intake (g)	5	81 ± 19[1]	84 ± 14	---	77 ± 10[de]
Total protein intake/kg body weight (g)	7	1.3 ± 0.4	1.5 ± 0.4	---	1.3 ± 0.3
Dietary protein intake/kg body weight (g)	7	1.3 ± 0.4	1.5 ± 0.4	---	1.3 ± 0.3
Lean body weight (kg)	7	53 ± 8[a]	54 ± 9[f]	54 ± 8[g]	55 ± 8[ah]
Arm-muscle circumference (cm)	7	23 ± 3	23 ± 3[k]	23 ± 3	23 ± 3[l]
Hair root diameter (mm x 10^{-2})	7	6 ± 1	7 ± 1	6 ± 3	7 ± 3
Anagen hair (%)	7	66 ± 11	64 ± 16	62 ± 13	72 ± 17
Serum albumin (g/100 ml)	7	3.9 ± 0.3	3.9 ± 0.4	4.0 ± 0.3	3.9 ± 0.6
Serum transferrin (mg/100 ml)	5	272 ± 74[b]	225 ± 87	195 ± 51	184 ± 41[b]
BUN (mg/100 ml)	7	96 ± 11[c]	87 ± 19	79 ± 12[c]	81 ± 18
Experimental group					
Total protein intake (g)	4	89 ± 17	103 ± 14	---	93 ± 10[d]
Total protein intake/kg body weight (g)	4	1.2 ± 0.2	1.4 ± 0.3	---	1.2 ± 0.2
Dietary protein intake (g)	4	86 ± 13	91 ± 20	---	91 ± 9[e]
Dietary protein intake/kg body weight (g)	4	1.1 ± 0.2	1.2 ± 0.3	---	1.2 ± 0.3
Lean body weight (kg)	3	65 ± 7[ij]	68 ± 7[f]	68 ± 7[gi]	68 ± 7[hj]
Arm-muscle circumference (cm)	3	26 ± 2	27 ± 1[k]	27 ± 1	28 ± 1[l]
Hair root diameter (mm x 10^{-2})	3	7 ± 1	6 ± 1	4 ± 4	7 ± 1
Anagen hair (%)	3	59 ± 15	70 ± 20[m]	59 ± 20[mn]	80 ± 15[n]
Serum albumin (g/100 ml)	4	4.1 ± 0.1	4.1 ± 0.2	4.1 ± 0.1	4.1 ± 0.1
Serum transferrin (mg/100 ml)	3	258 ± 58	192 ± 29	185 ± 26	183 ± 25
BUN (mg/100 ml)	4	84 ± 18	79 ± 11	76 ± 4	79 ± 17

[1] Values are mean ± standard deviation of mean.
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

and Erickson (42) studied 5 patients and found a mean protein intake of 50 g. The patients in the present study seemed to experience no difficulty in handling the higher intakes of protein.

Effect of Protein Intake on Parameters Assessing Protein Status

Lean body weight

Lean body weight includes the weight of the body cell mass plus skeletal and supporting tissues (75). The ability to maintain or increase lean body weight crudely implies adequate nutrition (13). Lean body weight ranged between 53-55 kg in the control group, with a significant increase ($P < 0.05$) noted between weeks 1 and 20 (Table IX). Lean body weight was greater in the experimental group and ranged between 65-68 kg. Significant increases ($P < 0.05$) were noted between weeks 1 and 12-13 as well as weeks 1 and 20 (Table IX). Thus protein intakes ranging from 77-84 g in the control group, and 89-103 g in the experimental group would seem to be adequate to meet daily protein needs for maintenance and repair, replace amino acid losses via hemodialysis, and to produce a significant increase in lean body weight. Energy intake would also seem to have been adequate.

Wilmore and Behnke (62) used the formula of Brozek et al. to calculate the lean body weight of 133 healthy men whose mean age, height and weight were 22 years, 177 cm, and 75.6 kg, respectively. Lean body weight was 64 $\pm$ 8 kg, with a range of 46-81 kg. The Brozek formula was used in this study to establish lean body weight, which ranged between 53-55 kg for the control group, and hence was approximately 10 kg less than the mean reported for healthy men studied by Wilmore and Behnke. Mean height and post-dialysis weight during week

20 was 171 cm and 62.3 kg, respectively (Table I). The control group had a greater proportion of the body as lean body weight than did the normal subjects studied by Wilmore and Behnke. The proportion as lean body weight in the experimental group was similar to that reported in normal men (Table IX). The lean body weight of both groups of subjects were thus normal for body size.

In the present study lean body mass, calculated as weight minus total body fat, varied from 87-88% for the control group and from 83-85% for the experimental group (Appendix Table 7). This compares favorably with the 84% found by Coles (28) for 6 hemodialysis patients and is well within the 75-85% range considered by him to be normal. Based on the work of Coles, 50 g of protein per day would seem to be sufficient to produce normal amounts of body protein in hemodialysis patients and thus the levels consumed in the present study would seem to be generously high.

Arm-muscle circumference

The arm-muscle circumference provides an indicator of the muscle content of the body, or its main protein reserve (68). Arm-muscle circumference of the control group was maintained at a constant level of 23 $\pm$ 3 cm, whereas values for the experimental group gradually increased from 26 $\pm$ 2 cm during week 1, to 28 $\pm$ 1 cm during week 20 (Table IX). Although no significant differences were observed with time, these trends would indicate a static reserve of muscle in the control group, and a progressive gain in muscle in the experimental group. Furthermore, during weeks 7-8 and 20, arm-muscle circumference of the experimental group was significantly greater ($P < 0.05$) than the

control group, and confirmed a similar increase in lean body weight (Table IX).

Jelliffe (66) calculated a "standard value" of 25.3 cm and a "90% standard value" of 22.8 cm for the arm-muscle circumference of healthy men. The arm-muscle circumference of the control group was less than the "standard value", and about equal to the "90% standard value". In the experimental group, arm-muscle circumference was consistently greater than the "standard value". As judged by arm-muscle circumference, protein reserves of the control group may be described as about 10% less than average, whereas protein reserves of the experimental group were greater than found in the average healthy male.

Hair root diameter

Mean bulb diameter is a sensitive indicator of body protein status because it responds promptly to protein deprivation and reverts to normal when protein is fed (71). Hair root, or mean bulb diameter ranged from 6-7 mm x 10^{-2} in the control group and from 4-7 mm x 10^{-2} in the experimental group (Table IX). No significant differences were found between or within groups.

Bradfield studied pre-school children with Asian and Negroid hair. He suggested that mean bulb diameters greater than 11 mm x 10^{-2} were indicative of normal protein-calorie nutrition, whereas bulb diameter between 6-11 mm x 10^{-2} were indicative of moderate protein-calorie malnutrition (70). These standards would indicate that both groups in the present study suffered from moderate protein-calorie malnutrition. This conclusion is not supported by other findings.

The control group consumed diets adequate in protein; and maintained normal values for per cent anagen hair and serum albumin; and slightly reduced, though still normal values for lean body weight and arm-muscle circumference. The experimental group also consumed diets adequate in protein and consistently maintained normal values for the other parameters.

Bradfield also studied the characteristics of hair in adult men. He reported a mean bulb diameter of 11.5 mm x 10^{-2} (range 8-14 mm x 10^{-2}) in 6 healthy men, aged 21-35 years (71). Only rarely in the present study were values found for individual subjects that fell within the lower region of the ranges found by Bradfield (Appendix Table 8). In several instances no well-formed bulbs were found and thus a reading of zero resulted. The low values found in the present study could be due to a difference in interpreting what Bradfield defined as a "well-formed bulb". Inspite of the low values observed, subjects were adequately nourished with protein.

Per cent anagen hair

Determination of the proportion of hair roots in the anagen or growing phase, is part of a rapid tissue technique used for the field assessment of protein-calorie malnutrition (70). The percentage of anagen hair in the control group ranged from 62-72% (Table IX), with no significant differences observed over time. The proportion of anagen hair in the experimental group ranged from 59-80%, with significant differences ($P < 0.05$) noted between weeks 7-8 and 12-13, and between weeks 12-13 and 20.

Bradfield considered the protein-calorie status of pre-school

children with Asian and Negroid hair to be normal when more than 50% of the hair roots examined microscopically were in the anagen or growing state. Application of this standard to the present data would indicate that the protein-calorie status of both the experimental and control groups was normal.

Serum albumin

Changes in serum albumin are useful in the diagnosis of protein depletion (80). In the present study, mean values for serum albumin ranged from 3.9-4.0 g/100 ml in the control group, and remained constant (4.1 g/100 ml) throughout the study in the experimental group (Table IX). No significant differences were found either within or between groups. Serum albumin levels ranging between 3.5-5.0 g/100 ml are considered normal.* Both the experimental and control groups had normal levels of albumin and were thus considered to be adequately nourished with protein when judged by this parameter.

Others have also found that serum albumin can be maintained at normal levels in hemodialysis patients when 3 times per week dialysis was combined with diets relatively high in protein of high biologic value. Fish and co-workers (8) fed an 80 g protein diet and found a mean serum albumin level of 4.4 g/100 ml, with values greater than 3.7 g/100 ml in all 46 patients studied. Pendras (13) found a mean albumin level of 4.4 g/100 ml (range 3.9-4.9 g/100 ml) and 4.5 g/100 ml (range 3.9-4.6 g/100 ml) in subjects consuming 60 and 80 g of protein, respectively.

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* As analyzed at the University of Alberta Hospital.

Serum transferrin

Serum transferrin is the B-globulin fraction of plasma proteins which is responsible for iron transport and can be used to assess protein-calorie status (26, 81). Serum transferrin levels of the control group gradually declined from a mean of 272 mg/100 ml during week 1, to 184 mg/100 ml during week 20 (Table IX). This difference was statistically significant ($P<0.05$). Serum transferrin levels of the experimental group also gradually declined from a mean of 258 mg/100 ml during week 1, to 183 mg/100 ml during week 20 (Table IX), but this difference was not statistically significant. No explanation can be offered as to why the levels dropped throughout the study.

Ooi and co-workers (26) observed transferrin levels in 38 healthy Caucasian subjects and 41 healthy Negro subjects, aged 20-60 years. A mean value of 314 mg/100 ml, with a range defined by 2 standard deviations of 176-453 mg/100 ml was observed. In the present study serum transferrin levels for all subjects ranged from 183-272 mg/100 ml. These levels fell within the range of 176-453 mg/100 ml calculated by Ooi et al. for normal healthy subjects (26).

The mean and range of serum transferrin values observed in the present study were comparable to, or greater than values reported in other groups of hemodialysis patients. Ooi and co-workers (26) investigated the interrelationship between serum transferrin and the nutritional state of 53 patients (aged 19-70 years) with chronic renal failure, including a group of 23 patients treated by maintenance hemodialysis or peritoneal dialysis. In these latter patients the mean transferrin level was 164 mg/100 ml (range 104-253 mg/100 ml). For

unknown reasons, decreased levels of serum transferrin were found by Ooi et al. in almost all patients with renal insufficiency (26). Young and Parsons (81) reported mean serum transferrin levels of 199 ± 141 mg/100 ml in 9 hemodialysis patients who received diets containing 50-80 g of protein daily, and who were dialyzed for 9 hours thrice weekly. This level was significantly lower ($P < 0.01$) than the corresponding mean and standard deviation of 348 ± 76 mg/100 ml observed in 12 normal control subjects (81). Serum transferrin levels were employed by Giordano et al. (82) to study the effects of histidine supplementation on 8 female and 12 male hemodialysis patients aged 8-51 years. Following consumption of ad libitum diets supplemented daily with 1 g of histidine for 9 weeks, serum transferrin levels significantly increased ($P < 0.01$) from about 205 ± 12 mg/100 ml to about 266 ± 14 mg/100 ml. The authors reported that a repletion of plasma histidine levels resulted in normal transferrin levels. In an abstract article, Müller and co-workers (83) found serum transferrin levels to be "nearly as low as in kwashiorkor", in hemodialysis patients consuming a 30-40 g protein diet of unselected quality. The levels of serum transferrin "normalized" within a few weeks following consumption of isocaloric diets containing a total of 60-80 g of protein, of which 60% was high quality.

The levels of serum transferrin of both the experimental and control groups in the present study were similar to those reported in studies of others. They are also within the range found for normal subjects. Ooi et al. (26) had observed that there was no direct relationship between serum levels of albumin and transferrin. This finding was confirmed in the present study.

Blood urea nitrogen (BUN)

Urea is the most important fraction of plasma non-protein nitrogen (72). Blood urea nitrogen values of the control group gradually declined from 96 ± 11 mg/100 ml during week 1, to 79 ± 12 mg/100 ml during weeks 12-13 (Table IX). This difference was statistically significant ($P<0.05$) and was due to a decrease in BUN values in all subjects except one. Blood urea nitrogen levels of the experimental group also gradually declined as the study progressed, but these changes were not significant.

BUN values ranging from 7 to 20 mg/100 ml are considered normal.* BUN values ranged from 96-79 mg/100 ml in the control group, and from 84-76 mg/100 ml in the experimental group (Table IX). As these values are considerably higher than normal, both groups would be considered to be uremic.

BUN levels of hemodialysis patients are influenced by several factors, including efficiency of the dialyzer, frequency and duration of dialysis, and the amount of protein ingested. A direct comparison of BUN values with other patient groups is difficult. Llach and co-workers (9) reported results of the use of MJ 7014 as the chief source of dietary amino acids and calories. Five hemodialysis patients and 5 patients with chronic renal failure who did not require dialysis, participated in a 4 week study. A daily intake of 50 g of protein and 4000 kcal was consumed by the hemodialysis patients. Pre-dialysis levels of BUN significantly decreased from 82 mg/100 ml to 35 mg/100 ml with the use of MJ 7014.

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* Criteria used at the University of Alberta Hospital.

Urea is removed with each dialysis and therefore Smith and Hill (14) felt that changes in BUN levels were more difficult to interpret in hemodialysis patients than in non-dialyzed patients. They compared successive pre-dialysis BUN levels of 3 hemodialysis patients and concluded that reduced levels were indicative of urea utilization for the synthesis of tissue protein (14). The significantly reduced ($P < 0.05$) BUN levels observed in the control group in this study may also be indicative of urea utilization for tissue synthesis. A significant increase ($P < 0.05$) in lean body weight of the control group between weeks 1 and 20 would support this conclusion. A gradual reduction in BUN levels and the concurrent increase ($P < 0.05$) in lean body weight could also indicate that the experimental group was utilizing urea for the synthesis of protein tissue. The possibility that greater utilization of endogenous urea for plasma protein and/or muscle tissue synthesis occurred in the experimental group would be supported by the following findings: lower levels of BUN; and higher levels of serum albumin, lean body weight and arm-muscle circumference.

IRON STATUS

Iron Intake

The control group consumed 12 $\pm$ 2 mg; 13 $\pm$ 4 mg and 12 $\pm$ 3 mg of iron during weeks 1, 7-8 and 20 respectively. These results were not statistically different (Table X). The experimental group consumed 16 $\pm$ 5 mg; 20 $\pm$ 1 mg; and 15 $\pm$ 4 mg of iron during the same weeks as the control group. These results were also not significantly different. During weeks 7-8, the experimental group consumed 20 $\pm$ 1 mg

TABLE X

The effect of nutritional supplementation on iron status of maintenance hemodialysis patients.

	n	Week 1	7-8	12-13	20
Control group					
Total iron intake (mg)	5	12 ± 2[1]	13 ± 4[c]	---	12 ± 3
Hemoglobin (g/100 ml)	6	8.0 ± 2.6	8.5 ± 3.9	7.9 ± 2.5	8.3 ± 2.5
Hematocrit (%)	6	22.9 ± 7.6	26.2 ± 11.9	22.8 ± 7.1	24.7 ± 7.9
Serum iron (ug/100 ml)	7	130 ± 47[a]	118 ± 64	113 ± 51	97 ± 23[a]
[2]T.I.B.C. (ug/100 ml)	7	275 ± 64	250 ± 41	251 ± 33	240 ± 26
[3]% SST (%)	7	50 ± 23[b]	48 ± 26	46 ± 23	41 ± 23[b]
Experimental group					
Total iron intake (mg)	4	16 ± 5	20 ± 1[cd]	---	15 ± 4
Dietary iron intake (mg)	4	14 ± 2	13 ± 2[d]	---	14 ± 3
Hemoglobin (g/100 ml)	4	9.4 ± 1.5	9.0 ± 1.8	9.0 ± 1.3	9.1 ± 1.2
Hematocrit (%)	4	28.1 ± 3.1	25.4 ± 3.3	26.8 ± 4.1	28.2 ± 4.0
Serum iron (ug/100 ml)	2	78 ± 54	101 ± 77	107 ± 85	116 ± 105
[2]T.I.B.C. (ug/100 ml)	2	235 ± 4	233 ± 10	224 ± 17	232 ± 8
[3]% SST (%)	2	33 ± 23	44 ± 35	47 ± 35	49 ± 44

[1]Values are mean ± standard deviation of mean.
[2]Total iron binding capacity, expressed as ug/100 ml.
[3]Per cent saturation of serum transferrin.
Values containing a common letter in their superscript are significantly different ($p < 0.05$).

of iron whereas the control group consumed 13 ± 2 mg which was statistically different ($P < 0.05$). This indicates that MJ 7014 can serve as a supplement, as MJ 7014 provided an additional 7 mg of iron to the mean intake of subjects in the experimental group. Dietary intake of iron, without the MJ 7014 supplement, was similar to the control group.

The 1974 Recommended Dietary Allowances (15) suggest a daily intake of 10 mg of iron for healthy adult males. In the present study, mean dietary intake ranged from 12-13 mg per day in the control group, and from 13-14 mg per day in the experimental group. These subjects consumed approximately 2100-2400 kcal per day from dietary sources, thus, the iron to energy ratio is similar to the 6 mg of iron/1000 kcal found in the average American diet (40).

Subjects participating in the present study consumed amounts of food iron similar to other dialysis patients reported in the literature. Pendras and Erickson (42) reported a mean daily intake of 11.7 mg of iron by 5 subjects consuming a diet containing 50 g of protein. Comty et al. (43) reported an intake of 9-11 mg per day by 15 subjects consuming a diet containing 60 g of protein. Twenty subjects eating a diet higher in energy and containing protein of high biologic value, obtained 12-16 mg of iron per day.

Effect of Iron Intake on Parameters Assessing Nutritional Status

Hemoglobin and hematocrit levels

Hemoglobin levels in the control group varied from 7.9-8.5 g/100 ml throughout the study (Table X). Hemoglobin levels of less than 12 g/100 ml in normal adult men were considered to be indicative

of anemia, by the Nutrition Canada Survey (84). Compared with this standard, all subjects in the control group would be considered to be severely anemic. This finding is also supported by low hematocrit levels, which varied from 22.8 to 26.2% (Table X). Hematocrit levels in healthy adult males range from 40-44% (48).

Hemoglobin and hematocrit levels were also low in the experimental group: hemoglobin levels varied from 9.0-9.4 g/100 ml, and hematocrit levels from 25.4-28.2% (Table X). Although these levels were slightly higher than levels in the control group, the differences were not statistically significant.

Low hemoglobin and hematocrit levels in maintenance hemodialysis patients have been frequently reported in the literature. Lawson and co-workers (47) reported a range in hemoglobin from 5.8-7.0 g/100 ml, with a mean level of 6.4 g/100 ml, in 11 patients who consumed a 40 g protein diet and had not received supplemental iron. Brozovich et al. (46) noted a mean hemoglobin level of 7.5 g/100 ml (range 5.2-8.7 g/100 ml) and a hematocrit level of 23% (range 19-28%) in 9 male patients who were not supplemented with iron. When 3 male patients with normal stores of marrow-iron, and 1 female and 2 male patients with iron-deficient stores, were supplemented for 3 months with a daily dose of 120 mg of elemental iron, Brozovich and co-workers found mean hemoglobin levels of 7.2 and 8.4 g/100 ml, respectively. Hematocrit levels for these same subjects were 22% and 25%, respectively (46). A mean hemoglobin level of 6.4 g/100 ml (range 3.3-10.6 g/100 ml), and a hematocrit level of 17.7% (range 9.9-32.2%) was reported by Strickland et al. (55) in 13 female and 21 male patients. Following supplementation with 100 mg of elemental iron per day for 12 weeks,

hemoglobin levels increased by 1.3 g/100 ml, and a statistically significant increase ($P < 0.05$) in hematocrit level occurred. Eschbach and co-workers (44) reported similar hematocrit levels in groups of male and female subjects regardless of iron status. They found hematocrit levels of 23% (range 16-33%) in 8 subjects considered to have a normal iron balance; 24% (range 19-31%) in 16 subjects who were iron deficient; and 21% (range 14-19%) in 10 subjects who were iron overloaded (44).

The higher levels for both hemoglobin and hematocrit found in subjects participating in this study, compared with levels reported in the literature, could be due to the use of de-ionized water instead of tap water as the dialysate diluent. Yawata and co-workers (52) found that replacement of tap water by de-ionized water resulted in a reduction in erythrocyte hemolysis and a corresponding increase in hematocrit levels by 5%.

Serum iron

Serum iron levels in the control group gradually decreased throughout the study, from 130 ug/100 ml during week 1, to 97 ug/100 ml during week 20 (Table X). This change was significantly different. The decrease was principally due to an excessive loss of blood which occurred in 3 subjects who lost varying amounts of blood during dialysis, when membranes in the dialyzer ruptured. One subject also encountered additional bleeding at the site of the fistula. Using the same chemical procedure for analysis* of iron as used in this study, values ranging

* Analysis for iron was done on a Technicon autoanalyzer, using a method employing the dye bathophenanthroline.

from 70-170 ug/100 ml are considered to be normal for the healthy adult male. The control group were not iron deficient, as judged by this parameter.

In contrast to the control group, levels of serum iron in the experimental group gradually increased throughout the study. The level at week 1 was 78 ug/100 ml and increased to 116 ug/100 ml at week 20 (Table X). The increase, which was not significant, was principally due to a gradual rise in the serum iron level of one subject. This subject, previous to participating in the study, had received a number of blood transfusions over several years and thus could have had ample body stores of iron to draw upon. The mean values for the experimental group also fell within the normal range of 70-170 ug/100 ml.

Levels of serum iron found for subjects participating in this study were generally higher than levels reported in other studies. Lawson and co-workers (47) reported a mean level of serum iron of 65 ug/100 ml (range 12-140 ug/100 ml) in 11 male subjects. Strickland et al. (55) reported serum levels of 67 ug/100 ml in 34 patients following consumption of a placebo for 12 weeks; and levels of 88 ug/100 ml in these same patients, following supplementation with 100 mg of elemental iron per day for 12 weeks. This increase was significant ($P<0.01$). Giordano and co-workers (82) found an initial mean level of 58 ug/100 ml in 8 female and 12 male patients, and a level of 87 ug/100 ml following supplementation with 1 g of histidine per day for 9 weeks. In the study conducted by Eschbach and co-workers (44) subjects considered to have normal iron status had plasma levels averaging 76 ug/100 ml (range 56-135 ug/100 ml); those who were iron-deficient had

levels of 47 ug/100 ml (range 31-64 ug/100 ml) and those with iron overload had levels of 197 ug/100 ml (range 133-261 ug/100 ml). Comty et al. (43) found levels averaging 139 ug/100 ml in 15 patients who consumed a diet containing 60 g of protein and 9-11 g of iron per day, and received 3.6 units of blood per month. Serum iron levels decreased to 80 ug/100 ml when these patients later consumed 12-16 mg of iron per day and received only 0.46 units of blood per month.

Total iron binding capacity (T.I.B.C.)

T.I.B.C for the control group, like serum iron levels, gradually decreased throughout the study. During week 1, the level was 275 ug/100 ml and this gradually decreased to 240 ug/100 ml during week 20 (Table X). This change was not significant. Normal values for healthy adult males range from 250-400 ug/100 ml* hence these subjects would be judged as "low-normal".

Little variation was observed in the levels of T.I.B.C. of the experimental group. Levels ranged from 235 ug/100 ml to 233, 224 and 232 ug/100 ml during weeks 1, 7-8, 12-13 and 20, respectively (Table X). Although these levels were lower than levels found in the control group, they were not statistically different. T.I.B.C. levels would indicate that the iron status of the experimental group was less than desirable.

Lawson et al. (47) reported a mean T.I.B.C. level of 335 ug/100 ml (range 175-561 ug/100 ml) in 11 male patients dialyzed 2 or 3 times per week. Brozovich et al. (46) reported similar levels of 325 ug/100 ml (range 246-542 ug/100 ml) in 9 male patients.

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* Analysis for T.I.B.C. was done on a Technicon autoanalyzer, using a method employing the dye bathophenanthroline.

Eschbach and co-workers (44) found that the more iron deficient patients were, the higher the T.I.B.C. levels. Thus, patients classified as iron-deficient had levels of 386 ug/100 ml (range 311-570 ug/100 ml); normal iron status, 250 ug/100 ml (213-329 ug/100 ml); and with iron overload, 241 ug/100 ml (196-299 ug/100 ml). Based on these criteria, subjects participating in the present study would appear to have ample body supplies of iron.

Per cent saturation of serum transferrin (%SST)

Per cent saturation of transferrin in the serum is calculated as a ratio of serum iron to total iron binding capacity, therefore, changes in either or both components will influence levels of % SST. Levels of T.I.B.C. in the control group were relatively unchanged throughout the study, whereas levels of serum iron decreased significantly ($P < 0.05$). Thus, the significant change which occurred in % SST of the control group was due to the decrease in levels of serum iron. Serum transferrin levels were 50, 48, 46 and 41% for weeks 1, 7-8, 12-13 and 20 respectively (Table X). Normal levels of % SST range from 20-50% (85), with values below 16% indicating iron-deficiency anemia (84, 85). Mean levels for the control group fell within the normal range.

The % SST levels of the experimental group were similarly affected by variations in serum iron levels, which increased throughout the study; T.I.B.C. levels remained relatively unchanged. Initial % SST levels were 33% for week 1, and gradually increased to 44, 47 and 49% during weeks 7-8, 12-13 and 20 respectively (Table X). These changes were not statistically significant, and mean values fell within normal range.

Eschbach et al. (44) again classified subjects as to iron deficient, normal or in overload iron status and reported % SST levels of 12%, 30% and 82% respectively. Thus, subjects in the present study had ample stores of iron as judged by % SST. Mean % SST values of 24% and 14% reported by Lawson et al. (47) and Brozovich et al. (46) were lower than the levels found in this study. Comty and co-workers (43) reported an average of 57% (range 34-83%) in 15 patients receiving 3.6 units of blood per month and a mean level of 28% (range 15-46%) when receiving 0.46 units per month.

Based on the parameters used in this study to judge the iron status of these subjects, they would be considered to be "anemic but not iron deficient" (46). Hemoglobin and hematocrit were less than normal range, whereas indicators of body iron stores such as serum iron levels, T.I.B.C. and % SST were normal. Failure of hemoglobin and hematocrit levels to be normal could be due to insufficient REF being produced by the diseased kidneys (30-32, 34). Inspite of sufficient body stores of iron, fewer number of erythrocytes were produced by the bone marrow than would be expected for the degree of anemia (29, 31, 34, 37).

Throughout the study many subjects in both the control and experimental groups were given iron dextran parenterally. It is estimated that the control group received about 430 mg of elemental iron per day by this route, and the experimental group received about 390 mg (Appendix Table 9). These amounts are so large compared with the 5-12 mg of iron obtained from consumption of MJ 7014 that any effect of the oral iron was not evident. As iron stores of subjects in this study were judged by several parameters to be normal, the amount

of parenteral iron given was sufficient to compensate for losses of blood due to: blood sampling; blood remaining in the dialyzer and blood lines at the end of each dialysis; rupturing of dialyzer membranes; and bleeding and/clotting of arterio-venous shunts.

GENERAL DISCUSSION

THE VALUE OF MJ 7014 AS A NUTRITIONAL SUPPLEMENT

MJ 7014 contains a source of energy; protein of high biologic value and a broad spectra of vitamins and minerals. Used as a supplement, this product had several advantages. It is packaged in sealed cans which simplified distribution to patients, as well as providing a rough measure of the amount consumed daily. Because the product is relatively soluble in hot or cold liquids it could be taken as a beverage, or combined with other foods. The orange and strawberry flavors were generally considered "acceptable".

The simultaneous intake of energy and protein of high biologic value could result in energy sparing protein. This could account for the increase in both total body and lean body weight, and the decrease in body fatness found in the experimental group. These changes occurred inspite of inter-current infections experienced by subjects 8, 9 and 10, and the re-cannulation surgery required by subjects 9 and 10. Three of the 4 patients said that they had "more strength" and "felt better" while consuming the supplement. Similar observations were reported by Llach and co-workers, who administered MJ 7014 to 5 MHD patients (9). One or more members of the experimental group said that they had noticed various other changes while consuming the supplement. They said that they had a better appetite; had increased their physical activity; had noticed a decrease in the "uremic taste" in the mouth; that their hair was softer in texture and was less likely to be spontaneously shed; and that their fingernails grew more rapidly. Some of the patients in the control group also noted similar

changes, but to a lesser extent.

MJ 7014 was not readily accepted by all patients. Acceptability of the product was partially responsible for the character of both the experimental and control groups. Several patients did not join the experimental group because they did not care for the "excessively sweet" taste of MJ 7014. This was also the reason given by some patients in the experimental group for decreasing consumption during the study. The quantity of liquid needed to dissolve the MJ 7014 powder also caused problems. The original directions state that 640 ml of water should be mixed with 1 can of powder. Daily consumption of this quantity resulted in undesirable weight gain and sensations of fullness, bloating and/or nausea. Patients usually used 120-480 ml of fluid for mixing, and consumed 1/3 to 3/4 of a can of powder per day.

Several patients in the experimental group failed to consume the supplement while ill, so that after the 11th week consumption of the group decreased. No one specific reason was given for stopping, but monotony of flavor, excessive sweetness and limited ways of serving the product were among the reasons given.

MJ 7014 was originally formulated as a liquid diet for renal patients. It contains sodium and potassium which are undesirable when used as a supplement. It also contains purified amino acids as a source of nitrogen which increases the cost of the product. Thus cost could limit the future use of MJ 7014 as a supplement by MHD patients.

THE NEED FOR BROAD SPECTRA NUTRITIONAL SUPPLEMENTATION BY MHD PATIENTS

Normal weight and adequate stores of body protein and fat are possible when MHD patients undergo dialysis 3 times per week and consume a nutritionally adequate diet. This was evident in the present study by the experimental group. Patients in this group began to gain weight while consuming the MJ 7014 supplement and deliberately decreased their consumption of the supplement to minimize weight gain. Patients who volunteered to participate in the control group might have benefited more from a nutritional supplement, but even they were relatively well nourished. If for some reason patients are not consuming a nutritionally adequate diet, are poorly nourished, have an inter-current infection, or must undergo frequent or extensive surgery, then the administration of a supplement could be of value. Subjects participating in the experimental group maintained their good nutritional status, even when subjected to severe infections or surgery. Consumption of the broad spectra supplements may have helped to buffer any deleterious effects of these stresses. Whether the experimental group would have done as well if they had not taken the supplements is unknown.

SUMMARY

Uremic patients undergoing maintenance hemodialysis (MHD) can be malnourished. The purpose of the present study was to assess the effect of broad spectra nutritional supplementation on the energy, protein and iron status of uremic patients undergoing MHD.

Seven and 4 men comprised the control and experimental groups, respectively. Both groups participated for 20 weeks and consumed their usual diet ad libitum. The experimental group also consumed MJ 7014 ad libitum, as well as vitamin supplements given in pill form. The control group were given placebo pills. Various parameters were used to assess the nutritional status of the subjects.

ENERGY STATUS

Total energy intake averaged 2100 kcal/day for the control group and varied from 2500 to 3300 kcal in the experimental group. This fluctuation was due to a variable intake of MJ 7014 by the experimental group. Throughout the study the experimental group gained approximately 3 kg. This weight gain could not be accounted for as body fat, since body fat decreased from 18 to 15%. Skinfold measurements and calculation of the cross-sectional fat area of the arm also indicated a decrease in body fatness. The control group gained about 1 kg throughout the study, with a slight decrease in body fat observed.

PROTEIN STATUS

Total protein intake ranged from 77-84 g/day and 89-103 g/day

for the control and experimental groups respectively. These subjects seemed to be able to metabolize the generous amounts of protein without adverse effect. BUN levels tended to be lower in the experimental group than in the control group. Three times per week dialysis likely enabled these patients to handle these larger amounts of protein. Lean body weight, arm-muscle circumference, percentage of hair in the anagen phase and serum albumin levels would suggest that protein status of both groups was adequate. BUN levels gradually decreased in both groups during the study and this could indicate some endogenous use of BUN for tissue protein synthesis. Three of 4 patients in the experimental group were subjected to stressful conditions such as infections and surgery. Protein status of this group remained good, inspite of these trauma. The high protein intake may have been responsible.

IRON STATUS

Iron intake was increased by 1-7 mg/day when MJ 7014 was consumed by the experimental group. Without the supplement, iron intake ranged from 12-14 mg/day in the control and experimental groups. Both hemoglobin and hematocrit levels were low compared with normal levels. Hemoglobin averaged approximately 8 g/100 ml in the control group and 9 g/100 ml in the experimental group with corresponding hematocrit levels of 25% and 27%. Although both groups were anemic they were not iron deficient as judged by serum iron, iron binding capacity, and per cent saturation of serum transferrin. Any possible supplementary benefit of oral iron administration was obscured by concommitant administration of parenteral iron.

THE NEED FOR BROAD SPECTRA NUTRITIONAL SUPPLEMENTATION BY MHD PATIENTS

The use of MJ 7014 as a supplement to the ad libitum diet of MHD patients was limited by the excessive sweetness of the product; monotony; amount of fluid needed to dissolve the product; and capacity of patients to consume the supplement. Future use could also be limited by the high cost of the supplement. Routine supplementation of MHD patients may not be necessary. Subjects in the present study were metabolically able to handle relatively generous intakes of protein when dialyzed 3 times/week. Many were able to maintain normal weight and adequate stores of body protein and fat while consuming a nutritionally adequate diet ad libitum. If for some reason patients are not consuming a nutritionally adequate diet, are malnourished, or subjected to extra stress of surgery or prolonged periods of infection, then a broad spectra supplement might be indicated.

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APPENDIX

TABLE 1

Activity schedule[1].

Activity	Pre-study	Week of Study 1-2	5-7	8-9	13	17	20	Post-study
Objective Assessment								
Dietary	E	C	E[2]	C, E[3]			C, E	
Anthropometric		C, E	C, E		C, E		C, E	
Biochemical		C, E	C, E	C, E	C, E	C, E	C, E	
Hair Morphology		C, E	C, E		C, E		C, E	
Subjective Assessment								
Diet & medical history			C, E					
Feedback questionnaire								C, E

[1] Control subjects = C; Experimental subjects = E.
[2] Subjects 10 and 11 recorded their 7-day intake.
[3] Subjects 8 and 9 recorded their 7-day intake.

TABLE 2

Instructions: food intake record.

THINK: Completeness, Accuracy!

1. Please record all food and fluid that you consume each day for seven days; beginning on Monday. Include all snack and nibble foods too. The only items that can be omitted are spices and water! Be as specific and descriptive as possible so that accurate calculations can be done later.

2. Accuracy is important too, in recording how much is eaten and drunk. Estimate amounts as closely as possible, using a standard measuring cup, spoons, or a ruler when in doubt.

3. Oil used in frying, flour or crumbs used in breading, or ingredients in food mixtures should also be indicated. Also the method of cooking, for example: broiled, baked, creamed. Please note under the "descriptive" column.

4. Please note if food has been lost due to vomiting. When possible estimate the amount.

5. Here are some examples of "how-to" record the food and drink of the day:

Food/fluid	Amount	Description
milk	2/3 c	homo
bran flakes	3/4 c	
sugar	2 tsp	white
pudding	1/2 c	home-made butterscotch
cream	1 tbsp	10% cream, poured on top pudding
beef stew	5-1" cubes beef 2 tbsp potato 1 small carrot 1/4 c chopped celery 1 tbsp gravy	
liver	about 3 oz raw	baked
flour	1 tsp	used to flour liver
oil	1 tsp	used to fry liver

TABLE 2 (Continued)

Food intake record.

Name_____ Study week no._____ Date_____

Time	Food/fluid item	Description	Amount
6:00 a.m. to 12:00 noon			
12:00 noon to 6:00 p.m.			
6:00 p.m. to 12:00 mid-night			
12:00 mid-night to 6:00 a.m.			

If taking the MJ powder please indicate:
1. amount consumed:
2. when consumed:
3. recipe or way consumed:

TABLE 3

Recipe Booklet Using Mead Johnson Product 7014

Developed and tested at the:

University of Alberta

School of Household Economics

Division of Foods and Nutrition

May, 1973.

TABLE 3 (Continued)

Beverages:

1. Each recipe yields 1 serving.

2. Each serving contains 2/3 cup of Mead Johnson 7014 powder, which is 1/4 of a can. Remember that you are required to take 1 can every day.

3. The fluid per serving is indicated for each recipe. Only the actual fluids in the recipe are included in the calculation. The powder is considered a solid food.

4. Although the Mead Johnson 7014 powder dissolves in cold water it dissolves more readily in warm water, and best in boiling water. Stirring, beating or blending helps too!

5. Cold beverages usually taste less-sweet than warm or hot ones.

6. To get the most nutrition in the least amount of fluid, add the Mead Johnson 7014 powder to water, tea, milk, juice, or any other beverage you drink. Then you count the fluid from these beverages and get the bonus of extra nutrition from the powder.

7. The beverages may be taken as an appetizer, with or after a meal, or in-between meals, or as a later-in-the evening "soother".

8. Three flavors are possible: orange, strawberry, or a blend of strawberry and orange. Try all three, for greater variety.

9. These beverage recipes are just some variations that are possible, using Mead Johnson 7014 orange and strawberry flavored powders. Experiment yourself! Create some new beverage recipes. Let's swap ideas!

MJ Drink

Yield: 1 serving
Fluid: 120 cc

Dissolve: 2/3 cup orange or strawberry MJ
in: 1/2 cup water (cold or hot)

Drink cold, or hot.

TABLE 3 (Continued)

MJ Orange Juice

Yield: 1 serving
Fluid: 120 cc

Dissolve: 2/3 cup of orange MJ
in: 1/2 cup orange juice

Serve chilled.

MJ Tea

Yield: 1 serving
Fluid: 120 cc

Brew tea to the strength you enjoy it (or stronger). Into your favorite cup pour: 1/2 cup hot tea

Stir to dissolve: 2/3 cup orange MJ

Enjoy hot, garnished with a cinnamon stick.

Variation: Vitaminized iced tea:

Brew tea to double strength. Chill. Then add the MJ powder in above amounts. Serve over ice with a lemon slice.

MJ Eggnog

Yield: 1 serving
Fluid: 150 cc

Beat until thick: 1 egg

Add: 1/4 cup milk
Dash nutmeg

Gradually beat in: 2/3 cup orange or strawberry MJ

Enjoy it chilled as a night-time drink or at breakfast.

TABLE 3 (Continued)

MJ Milkshake

Yield: 1 serving
Fluid: 200 cc

Combine together by beating: 1/2 cup milk
2/3 cup orange or strawberry MJ
1 scoop vanilla ice-cream

Variations: 1. Use 1/3 cup orange MJ and 1/3 cup strawberry MJ

2. Use different flavors of ice-cream.

MJ Soda

Yield: 1 serving
Fluid: 200 cc

Stir to dissolve: 2/3 cup orange or strawberry MJ
in: 1/4 cup chilled pop

Pour this syrup into a tall glass, then:

Add: 1 scoop vanilla ice-cream

Top with: 1/4 cup chilled pop

Sip with 2 straws!

Variations: MJ soda with:

1. 1/3 cup orange MJ + 1/3 cup strawberry MJ
2. Different flavors of ice-cream
3. Pop: gingerale, lemon-lime, orange, grape
4. Soda water or tonic water.

TABLE 3 (Continued)

Desserts

1. Each recipe yields 1 serving (1/4 can or 2/3 cup of MJ) or
   2 servings (1/2 can or 1¼ cups of MJ)

   Remember that with each serving you consume 1/4 of a can. However, in a day you are required to consume 1 can.

2. The fluid per 1 serving is indicated for each recipe. Only the actual fluids used in the recipe are included in the calculation.

3. Because the Mead Johnson product is intended as a supplement, it is hoped that these desserts will be taken as extras, not in place of your regular desserts. For a good compromise, add your fruit or other dessert to these recipes. More nutrition less bulk!

4. During the weeks when you are required to record your food intake please indicate which recipe variation you consumed. For example: 1 serving MJ cream with 1/2 cup sliced fresh strawberries.

MJ Popsicle

Yield: 1 serving
Fluid: 180 cc

Dissolve: 2/3 cup orange or strawberry MJ
in: 3/4 cup boiling water

Pour into refrigerator tray or popsicle mold
Freeze until solid.

MJ Yoghurt

Yield: 1 serving
Fluid: 60 cc

Several hours before serving blend: 2/3 cup orange or strawberry MJ
in: 1/4 cup vanilla yoghurt

Chill before serving.

Variations: 1. MJ Yoghurt using strawberry yoghurt
2. MJ Yoghurt using orange yoghurt
3. Experiment with other flavors of yoghurt.

TABLE 3 (Continued)

MJ Jelly

Yield: 2 servings
Fluid per serving: 100 cc

Soften: 1 tablespoon unflavored gelatin
in: 2 tablespoons cold water

Dissolve: 1¼ cups orange or strawberry MJ
in: 2/3 cup boiling water
add: 1 tablespoon lemon juice

Combine gelatin and syrup stirring until dissolved.
Rinse 2 molds or serving dishes with cold water.
Pour gelatin mixture into dishes. Chill until firm.

Variations:
1. MJ jelly with cream
2. MJ jelly with custard sauce
3. MJ jelly with ice-cream
4. MJ jelly garnished with fruit
5. MJ jelly with fruit folded into jelly when it is partially set
6. MJ fruit juice jelly--use 1/3 cup fruit juice instead of 1/3 cup boiling water
7. MJ milk jelly--use 1/3 cup milk instead of 1/3 cup boiling water
8. MJ Bavarian jelly--use 1/3 cup whipped cream instead of 1/3 cup boiling water.

MJ Cream

Yield: 1 serving
Fluid: 60 cc

In a refrigerator bowl blend: 2/3 cup orange or strawberry MJ
in: 1/4 cup sour cream

Chill before serving.

Variations:
1. MJ Cream with fruits folded into it
2. MJ cream made with 1/3 cup strawberry MJ and 1/3 cup orange MJ.

TABLE 3 (Continued)

MJ Fluffy Dessert

Yield: 2 servings
Fluid per serving: 75 cc

In a saucepan soften: 1 tablespoon unflavored gelatin
in: 1/4 cup cold water

Then heat, gradually adding: 1 cup orange or strawberry MJ
Stir until dissolved
Remove from heat.

In a bowl beat until frothy: 1 egg yolk
add: 1 tablespoon water
and: 1/4 cup orange or strawberry MJ

Beat until thick.
Add some of the hot gelatin mixture to egg yolk. Mix and add to remaining gelatin mixture. Cook until thickened, stirring constantly. Cool slightly.

Beat until stiff peaks form: 1 egg white

Fold yolk mixture into beaten egg white. Pour into serving dishes. Chill.

Variation: MJ Fluffy Dessert with fruit: fold fruit into the dessert when combining the egg yolk and egg white mixtures.

MJ Plain Sherbet

Yield: 2 servings
Fluid per serving: 120 cc

Dissolve: 1¼ cup orange or strawberry MJ
in: 1 cup boiling water

Pour into refrigerator tray.
Freeze until partially set, then, remove from tray to bowl. Using egg beater or hand mixer, beat until fluffy. Freeze.

Variations: 1. MJ Plain Sherbet with Egg White:
Beat 1 egg white to almost stiff peak stage. Fold partially frozen beaten sherbet into beaten egg white. Then refreeze.

2. MJ Plain Sherbet with 3/4 cup orange MJ powder + 1/3 cup strawberry MJ powder (or vice-versa).

TABLE 4

HEMODIALYSIS NUTRITION STUDY.

DIETARY/MEDICAL HISTORY QUESTIONNAIRE.

I. Personal history:

Name _____ Marital Status ____

Birthdate _____ Occupation _____

II. Etiology of chronic renal failure:

Diagnosis

Approximate date of diagnosis

III. Pertinent history:

A. Before the onset of kidney disease:

Height

Weight

General state of health

Appetite

Medications/vitamins--approximate length of time.

Were food habits and intake different from today?

TABLE 4 (Continued)

B. With kidney disease but before beginning the hemodialysis program:

Weight

Surgery required

Medical problems

Medications/vitamins--indicate length of time and dosage

Special diet required?

If yes:

Diet order(s)

Date when ordered

Date when discontinued

Comments

TABLE 4 (Continued)

C. With kidney disease and peritoneal dialysis (if applicable):

Approximate dates of peritoneal dialysis

Number of peritoneal dialysis requires:

Per week

Totally

Hours per dialysis treatment

Weight

Effect of peritoneal dialysis on state of well-being

Medications/vitamins--indicate length of time and dosage

Special diet required? Able to follow?

Comments

TABLE 4 (Continued)

D. With kidney disease and on the hemodialysis program:

No. of months on dialysis

Date of 1st dialysis

Weight at 1st dialysis

Reference "dry weight" today

Usual number of:

	Now	Duration	Past	Duration
Dialysis per week				
Hours per dialysis treatment				

Type of kidney machine usually used for dialysis

Cannula or A-V fistula

What effect does hemodialysis have on (1) usual state of well-being (2) food intake and (3) ability to keep food down:

Just before dialysis

During dialysis

After dialysis

Between dialyses

Additional comments

TABLE 4 (Continued)

D. With kidney disease and on the hemodialysis program:

Diets prescribed (Kcal Pro Na^+ K^+)	Length of time required	Comments

TABLE 4 (Continued)

IV. Initial and past drug therapy:

Medication	No	Yes	Dosage	Duration	Comments
Multivitamins (specify)					
Iron					
Folic Acid					
Vitamin D					
Dihydroxytachysterol					
Calcium					
Other vitamins or minerals (specify)					
Phosphate-Binding Agent					
Potassium-Binding Agent					
Anti-coagulant					
Anti-epileptic drug					
Cortisone					
Testosterone					
Other (specify)					

TABLE 5

Feedback questionnaire.

I. Overall opinions.

II. Health, physical activity and events relating to hemodialysis during the study period.

III. Opinions regarding the parameters used during the study:

A. Anthropometric:

1. Weight.

2. Mid-arm circumference.

3. Skinfold calipration.

B. Biochemical:

1. Amount of blood sampling required.

2. Blood loss.

C. Hair biopsy.

D. 7-day food and fluid intake record.

IV. Opinions and recommendations regarding the nutritional supplements used:

A. Vitamin and mineral supplement, placebo.

B. MJ 7014.

V. Additional comments and suggestions.

TABLE 6

Consumption of MJ 7014 by the experimental group.

Subject	Began Week	Discontinued Week	Discontinued Reason	Quantity Frequently Consumed Proportion of 1 can
8	1	11	Hospitalization	3/4
9	1	13	Hospitalization	1/2
10	1	16	Hospitalization	1/2
11	1	20	End of study	1/3-1/2
$\bar{X}$	1	15	--	--

TABLE 7

Lean body mass[1], expressed as % of post-dialysis weight[2].

Subject	Week 1	7-8	12-13	20
Control group				
1	91	91	91	91
2	87	86	88	88
3	87	87	88	87
4	88	87	87	86
5	81	82	83	83
6	91	92	92	92
7	86	87	89	87
$\bar{X} \pm SD$	87 ± 3	87 ± 3	88 ± 3	88 ± 3
Experimental group				
8	85	85	Missing	87
9	87	94	91	91
10	76	76	79	79
11	82	85	85	83
$\bar{X} \pm SD$	83 ± 5	85 ± 7	85 ± 6	85 ± 5

[1]Calculated by the formula: Lean body mass = Post-dialysis Weight - Total Body Fat.
[2]Tests of significance were not calculated.

TABLE 8

Mean hair root (anagen) diameter.

Subject	Mean hair root diameter (mm x 10^{-2})			
	Week			
	1	7-8	12-13	20
Control group				
1	6	8	6	7
2	6	6	6	6
3	7	6	10	9
4	6	6	7	8
5	7	8	7	8
6	6	7	8	9
7	4	5	0	0
$\bar{X} \pm SD$	6 ± 1	7 ± 1	6 ± 3	7 ± 3
Experimental group				
8	8	7	Missing	9
9	6	6	6	7
10	7	6	6	6
11	7	5	0	8
$\bar{X} \pm SD$	7 ± 1	6 ± 1	4 ± 4	8 ± 1
[1]$\bar{X} \pm SD$	7 ± 1	6 ± 1	4 ± 4	7 ± 1

[1]The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences.

TABLE 9

Elemental iron received parenterally as iron dextran[1].

Subject	Week				
Control group	1	7-8	12-13	20	1-20 inclusive[2]
1	-	-	-	-	-
2	5,000	5,000	5,000	5,000	100,000
3	-	5,000	5,000	5,000	90,000
4	5,000	5,000	5,000	5,000	85,000
5	5,000	5,000	5,000	5,000	90,000
6	5,000	-	-	-	20,000
7	-	-	5,000	5,000	45,000
$\bar{X}$ per week	2,857	2,857	3,571	3,571	61,429
$\bar{X}$ per day	408	408	510	510	439
Experimental group					
8	5,000	5,000	-	5,000	60,000
9	-	-	-	-	-
10	5,000	5,000	5,000	-	60,000
11	5,000	5,000	5,000	5,000	100,000
$\bar{X}$ per week	3,750	3,750	2,500	2,500	55,000
$\bar{X}$ per day	535	535	357	357	393

[1] Expressed as mg of elemental iron.
[2] Cumulative intake of elemental iron throughout the study.

TABLE 10

Total energy intake[1] provided daily by diet and MJ 7014, and proportion of total intake supplied by MJ 7014.

Subject	Week 1				Week 7-8				Week 20			
	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ
Control group												
1	Missing	--	Missing	--	2650 ± 584	--	2650 ± 584	--	2080 ± 345	--	2080 ± 345	--
2	2540 ± 541	--	2640 ± 541	--	2060 ± 1006	--	2060 ± 1006	--	1900 ± 704	--	1900 ± 704	--
3	1860 ± 620	--	1860 ± 620	--	1790 ± 398	--	1990 ± 398	--	1670 ± 267	--	1670 ± 267	--
4	2710 ± 309	--	2710 ± 309	--	2870 ± 784	--	2870 ± [illegible]4	--	2380 ± 485	--	2380 ± 485	--
5	1580 ± 642	--	1580 ± 642	--	1750 ± 551	--	1750 ± 551	--	1670 ± 517	--	1670 ± 517	--
6	2110 ± 772	--	2110 ± 772	--	2270 ± 410	--	2270 ± 410	--	2740 ± 551	--	2740 ± 551	--
7	2190 ± 415	--	2190 ± 415	--	Missing	--	Missing	--	2830 ± 334	--	2830 ± 334	--
$\bar{X}$ ± SD	2170 ± 417	--	2170 ± 417	--	2270 ± 423	--	2270[a] ± 423	--	2180 ± 481	--	2180 ± 481	--
$^2\bar{X}$ ± SD	2160 ± 466	--	2160 ± 466	--	2190 ± 423	--	2190 ± 423	--	2070 ± 474	--	2070 ± 474	--
Experimental group												
8	1630 ± 258	*	1630 ± 258	--	1990 ± 295	730 ± 684	2720 ± 295	30	1970 ± 261	--	1970 ± 261	--
9	3580 ± 700	*	3580 ± 700	--	3100 ± 783	800 ± 0	3900 ± 783	20	3610 ± 475	--	3610 ± 475	--
10	2560 ± 636	*	2560 ± 636	--	1890 ± 487	1600 ± 0	3490 ± 487	50	1900 ± 536	--	1900 ± 536	--
11	2180 ± 530	1030 ± 761[3]	3210 ± 791	30	2500 ± 481	630 ± 315	3130 ± 481	20	2140 ± 235	510 ± 302	2650 ± 235	20
$\bar{X}$ ± SD	2490 ± 820	260 ± 515	2740 ± 855	8 ± 16	2370[b] ± 556	940 ± 446	3310[ab] ± 501	30 ± 12	2410 ± 805	130 ± 257	2540 ± 789	5 ± 10

[1] Units in kcal; values expressed as $\bar{X}$ ± SD.
[2] The $\bar{X}$ ± SD of subjects 2-6. Used in the paired 't' test to determine significant differences.
[3] MJ 7014 was consumed on a trial basis.
* Actual intakes recorded previous to week 1 (Appendix Table 1).
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 11

Energy intake per kilogram body weight[1].

Subject	Week 1		Weeks 7-8		Week 20	
Control group	Total intake	Dietary intake	Total intake	Dietary intake	Total intake	Dietary intake
1	Missing	Missing	51	51	38	38
2	49	49	38	38	38	38
3	24	24	25	25	22	22
4	45	45	46	46	38	38
5	23	23	25	25	24	24
6	41	41	45	45	53	53
7	32	32	Missing	Missing	42	42
$\bar{X} \pm SD$	36 ± 11	36 ± 11	39 ± 11	39 ± 11	36 ± 11	36 ± 11
Experimental group						
8	26	26	43	31	29	29
9	52	52	57	45	53	53
10	31	31	42	23	23	23
11	36	25	37	28	29	23
$\bar{X} \pm SD$	36 ± 11	33 ± 13	44 ± 9	32 ± 10	33 ± 13	32 ± 14

[1] Values are expressed as kcal/kg.
Tests of significance were not calculated for this data.

TABLE 12

Post-dialysis weight and % body fat[1].

Subject	Post-dialysis weight (kg)				Body fat (%)			
	Week				Week			
	1	7-8	12-13	20	1	7-8	12-13	20
Control group								
1	50.8	52.6	53.5	54.4	9	9	9	9
2	51.4	51.8	51.4	50.5	13	14	12	12
3	76.6	78.6	75.0	76.9	13	13	12	13
4	60.2	62.5	61.9	63.4	12	13	13	14
5	69.2	70.1	71.4	71.3	19	18	17	17
6	52.0	50.7	50.9	51.4	9	8	8	8
7	67.8	67.6	67.5	68.3	14	13	11	13
$\bar{X} \pm SD$	61.1±10.3	62.0±10.7	61.7^{d}±10.0	62.3^{e}±10.4	13±3	13±3	12±3	12±3
Experimental group								
8	63.5	64.1	71.2	68.8	15	15	Missing	13
9	69.0	69.0	68.8	68.6	13	6	9	9
10	82.2	83.6	83.6	85.0	24	24	21	21
11	89.1	90.3	90.2	92.0	18	15	15	17
$\bar{X} \pm SD$	76.0±11.8	76.8±12.3	78.5^{d}±10.2	78.6^{e}±11.8	17±5	15±7	15±6	15±5
[2] $\bar{X} \pm SD$	--	--	--	--	18^{c}±16	15±9	15^{c}±6	16±6

[1]Body fat was calculated using the formulae:

Density = 1.0950 - 0.0015 (Triceps skinfold thickness) - 0.0012 (Sub-scapula skinfold thickness)(67).

$$\% \text{ Body fat} = \left[\frac{4.570}{\text{Density}} - 4.142\right] \times 100 \quad (62).$$

[2]The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 13

Skinfold measurements

Subject	Triceps (mm) Week 1	7-8	12-13	20	Sub-scapula (mm) Week 1	7-8	12-13	20	Triceps + Sub-scapula (mm) Week 1	7-8	12-13	20
Control group												
1	6	6	6	7	5	4	5	5	11	10	11	12
2	8	7	6	7	12	15	12	10	20	22	18	17
3	11	11	10	12	7	6	6	6	18	17	16	18
4	9	9	9	10	8	10	10	10	17	19	19	20
5	14	13	13	13	15	15	14	14	29	28	27	27
6	5	5	4	5	7	6	5	5	12	11	9	10
7	9	8	6	8	12	11	9	10	21	19	15	18
$\bar{X} \pm SD$	9 ± 3	8 ± 3	$8^{e} \pm 3$	$9^{e} \pm 3$	$9^{c} \pm 4$	10 ± 4	9 ± 4	9 ± 3	18 ± 16	18 ± 6	16 ± 6	17 ± 6
Experimental group												
8	7	9	Missing	8	16	14	Missing	11	23	23	Missing	19
9	9	6	6	5	9	7	6	6	18	13	12	11
10	17	15	15	14	22	24	20	21	39	39	35	35
11	10	9	8	9	19	15	16	19	29	24	24	28
$\bar{X} \pm SD$	11 ± 4	10 ± 4	10 ± 5	9 ± 4	$17^{c} \pm 6$	15 ± 7	14 ± 7	14 ± 7	27 ± 9	25 ± 11	24 ± 12	23 ± 10
[1] $\bar{X} \pm SD$	$12^{b} \pm 4$	10 ± 5	$10^{b} \pm 5$	9 ± 5	$17^{d} \pm 7$	15 ± 9	$14^{d} \pm 7$	15 ± 8	$29^{af} \pm 11$	25 ± 13	$24^{a} \pm 12$	$25^{f} \pm 12$

[1] $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 14

Cross-sectional fat area[1].

Subject	Week			
	1	7-8	12-13	20
Control group				
1	6	6	6	8
2	9	7	6	8
3	12	12	10	13
4	10	10	10	11
5	10	15	15	15
6	5	4	3	5
7	10	8	7	9
$\bar{X} \pm SD$	9 ± 2	$9^{ac} \pm 4$	$8^{bc} \pm 4$	$10^{ab} \pm 3$
Experimental group				
8	7	10	Missing	9
9	10	7	7	5
10	20	20	20	19
11	12	13	11	12
$\bar{X} \pm SD$	12 ± 6	13 ± 6	13 ± 7	11 ± 6
[2]$\bar{X} \pm SD$	14 ± 5	13 ± 7	13 ± 7	12 ± 7

[1]Cross-sectional fat area is equal to arm area minus muscle area, and was determined by nomogram (68). Values are expressed in cm^2.

[2]The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 15

Proportion of hair in the telogen phase (%).

Subject	Week 1	7-8	12-13	20
Control group				
1	12	25	28	18
2	13	26	44	26
3	36	39	44	11
4	17	16	22	10
5	6	2	4	4
6	21	9	23	9
7	22	17	23	34
$\bar{X} \pm SD$	18 ± 10	$19^b \pm 12$	$27^b \pm 14$	16 ± 11
Experimental group				
8	8	0	Missing	4
9	16	6	18	4
10	33	20	37	12
11	38	22	25	3
$\bar{X} \pm SD$	24 ± 14	12 ± 11	26 ± 10	6 ± 4
[1] $\bar{X} \pm SD$	$29^a \pm 12$	$16^a \pm 9$	$26^c \pm 10$	$6^c \pm 5$

[1] The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 16

Protein intake[1] provided daily by diet and MJ 7014, and proportion of total intake supplied by MJ 7014.

Subject	Week 1				Week 7-8				Week 20			
	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ
Control group												
1	Missing	--	Missing	--	103 ± 22	--	103 ± 22	--	78 ± 19	--	78 ± 19	--
2	91 ± 22	--	91 ± 22	--	63 ± 27	--	63 ± 27	--	83 ± 27	--	83 ± 27	--
3	78 ± 20	--	78 ± 20	--	89 ± 8	--	89 ± 8	--	65 ± 14	--	65 ± 14	--
4	103 ± 24	--	103 ± 24	--	95 ± 31	--	95 ± 31	--	84 ± 18	--	84 ± 18	--
5	51 ± 17	--	51 ± 17	--	75 ± 20	--	75 ± 20	--	68 ± 28	--	68 ± 28	--
6	80 ± 16	--	80 ± 16	--	96 ± 19	--	96 ± 19	--	86 ± 20	--	86 ± 20	--
7	67 ± 12	--	67 ± 12	--	Missing	--	Missing	--	71 ± 18	--	71 ± 18	--
$\bar{X}$ ± SD	78 ± 18	--	78 ± 18	--	87 ± 15	--	87 ± 15	--	76 ± 9	--	76 ± 9	--
[2]$\bar{X}$ ± SD	81 ± 19	--	81 ± 19	--	84 ± 14	--	84 ± 14	--	77^{a} ± 10	--	77^{b} ± 10	--
Experimental group												
8	69 ± 11	*	69 ± 11	--	93 ± 18	10 ± 9	103 ± 18	9	88 ± 12	--	*88 ± 12	--
9	95 ± 14	*	95 ± 14	--	95 ± 11	11 ± 0	106 ± 11	9	104 ± 16	--	104 ± 16	--
10	84 ± 24	*	84 ± 24	--	64 ± 12	21 ± 0	85 ± 12	25	82 ± 14	--	82 ± 14	--
11	95 ± 39	14[3] ± 10	109 ± 36	12	112 ± 22	8 ± 4	120 ± 22	7	91 ± 25	7 ± 4	98 ± 26	7
$\bar{X}$ ± SD	86 ± 13	4 ± 7	89 ± 17	3 ± 6	91 ± 20	12 ± 6	103 ± 14	13 ± 8	91^{a} ± 9	2 ± 4	93^{b} ± 10	2 ± 3

[1] Expressed in grams.
[2] The $\bar{X}$ ± SD of subjects 2, 3, 4, 5, and 6. Used in the paired 't' test to determine significant differences.
[3] MJ 7014 was consumed on a trial basis.
*Actual intakes recorded previous to week 1 (Appendix Table 1).
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 17

Protein intake per kilogram body weight[1].

Subject	Week 1		Weeks 7-8		Week 20	
Control group	Total intake	Dietary intake	Total intake	Dietary intake	Total intake	Dietary intake
1	Missing	Missing	2.0	2.0	1.4	1.4
2	1.8	1.8	1.2	1.2	1.6	1.6
3	1.0	1.0	1.1	1.1	0.8	0.8
4	1.7	1.7	1.5	1.5	1.3	1.3
5	0.7	0.7	1.1	1.1	1.0	1.0
6	1.5	1.5	1.9	1.9	1.7	1.7
7	1.0	1.0	Missing	Missing	1.0	1.0
$\bar{X} \pm SD$	1.3 ± 0.4	1.3 ± 0.4	1.5 ± 0.4	1.5 ± 0.4	1.3 ± 0.3	1.3 ± 0.3
Experimental group						
8	1.1	1.1	1.6	1.5	1.3	1.3
9	1.4	1.4	1.5	1.4	1.5	1.5
10	1.0	1.0	1.0	0.8	1.0	1.0
11	1.2	1.1	1.3	1.2	1.1	1.0
$\bar{X} \pm SD$	1.2 ± 0.2	1.1 ± 0.2	1.4 ± 0.3	1.2 ± 0.3	1.2 ± 0.2	1.2 ± 0.3

[1] Values are expressed as g/kg.
Tests of significance were not calculated for this data.

TABLE 18

Lean body weight[1].

Subject	Week 1	7-8	12-13	20
Control group				
1	46	48	49	49
2	45	45	45	45
3	67	69	66	67
4	53	54	54	55
5	56	58	59	59
6	47	46	47	47
7	58	59	60	60
$\bar{X} \pm SD$	$53^{a} \pm 8$	$54^{b} \pm 9$	$54^{c} \pm 8$	$55^{ad} \pm 8$
Experimental group				
8	54	55	Missing	60
9	60	65	62	62
10	63	64	66	67
11	73	76	76	76
$\bar{X} \pm SD$	62 ± 8	$65^{b} \pm 9$	$68^{c} \pm 7$	$66^{d} \pm 7$
[2]$\bar{X} \pm SD$	$65^{ef} \pm 7$	68 ± 7	$68^{f} \pm 7$	$68^{e} \pm 7$

[1]Lean body weight is expressed in kg, and was calculated as follows (62):
Lean body weight = post-dialysis weight - (post-dialysis weight x % body fat).
[2]The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 19

Arm-muscle circumference[1].

Subject	Week			
	1	7-8	12-13	20
Control group				
1	18	18	19	18
2	25	25	25	24
3	21	22	22	22
4	23	23	24	24
5	26	25	26	25
6	23	23	23	23
7	26	26	26	27
$\bar{X} \pm SD$	23 ± 3	$23^{a} \pm 3$	23 ± 3	$23^{b} \pm 3$
Experimental group				
8	24	24	Missing	24
9	26	27	27	28
10	24	27	26	27
11	27	28	28	28
$\bar{X} \pm SD$	25 ± 1	$26^{a} \pm 2$	27 ± 1	$26^{b} \pm 2$
[2]$\bar{X} \pm SD$	26 ± 2	27 ± 1	27 ± 1	28 ± 1

[1] A nomogram was used to determine arm-muscle circumference values, which are expressed in cm.
[2] The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 20

Proportion of hair in the anagen phase (%).

Subject	Week 1	7-8	12-13	20
Control group				
1	76	42	60	58
2	71	66	52	74
3	49	54	52	82
4	75	59	72	80
5	74	90	86	94
6	63	78	66	73
7	52	57	49	43
$\bar{X} \pm SD$	66 ± 11	64 ± 16	62 ± 13	72 ± 17
Experimental group				
8	70	82	Missing	70
9	76	92	80	94
10	52	52	40	65
11	48	67	57	80
$\bar{X} \pm SD$	62 ± 14	73 ± 18	59 ± 20	77 ± 13
[1] $\bar{X} \pm SD$	59 ± 15	70^{a} ± 20	59^{ab} ± 20	80^{b} ± 15

[1] The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences. Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 21

Serum albumin and transferrin levels.

Subject	Serum albumin (g/100 ml) Week				Serum transferrin (mg/100 ml) Week			
Control group	1	7-8	12-13	20	1	7-8	12-13	20
1	4.1	4.2	4.0	4.2	275	180	156	200
2	4.2	4.0	3.7	3.9	350	200	Missing	215
3	4.2	4.3	4.2	4.4	330	280	185	215
4	4.3	3.9	4.2	4.1	Missing	225	208	165
5	3.7	3.9	4.0	4.0	300	200	200	215
6	3.6	3.6	3.5	2.9	310	344	280	173
7	3.7	3.4	4.2	4.1	145	123	156	117
$\bar{X} \pm SD$	4.0±0.3	3.9±0.3	4.0±0.3	3.9±0.5	285±73	222±72	198±46	186±37
[1] $\bar{X} \pm SD$	3.9±0.3	3.9±0.4	4.0±0.3	3.9±0.6	272[a]±74	225±87	195±51	184[a]±41
Experimental group								
8	3.7	3.6	3.0	3.4	Missing	276	255	215
9	4.1	3.9	4.1	4.0	260	200	190	165
10	4.0	4.1	4.1	4.2	315	216	208	212
11	4.1	4.2	4.0	4.2	200	159	156	173
$\bar{X} \pm SD$	4.0±0.2	4.0±0.3	3.8±0.5	4.0±0.4	258±58	213±49	202±41	191±26
[2] $\bar{X} \pm SD$	4.1±0.1	4.1±0.2	4.1±0.1	4.1±0.1	258±58	192±29	185±26	183±25

[1] The $\bar{X} \pm SD$ of subjects 1, 3, 5, 6, 7. Used in the paired 't' test to determine significant differences.
[2] The $\bar{X} \pm SD$ of subjects 9, 10 and 11. Used in the paired 't' test to determine significant differences.
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 22

Blood urea nitrogen levels[1]

Subject	Week 1	7-8	12-13	20
Control group				
1	85	106	86	114
2	88	90	83	86
3	108	104	95	64
4	96	69	76	86
5	114	61	71	71
6	86	76	58	63
7	93	104	86	82
$\bar{X} \pm SD$	$96^{a} \pm 11$	87 ± 19	$79^{a} \pm 12$	81 ± 18
Experimental group				
8	110	78	82	104
9	82	79	73	67
10	68	67	76	79
11	76	93	74	67
$\bar{X} \pm SD$	84 ± 18	79 ± 11	76 ± 4	79 ± 17

[1] Values are expressed as mg/100 ml.
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 23

Iron intake[1] provided daily by diet and MJ 7014, and proportion of the total intake supplied by MJ 7014.

Subject	Week 1				Week 7-8				Week 20			
	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ	Diet	MJ	Total	% MJ
Control group												
1	Missing	--	Missing	--	15 ± 4	--	15 ± 4	--	12 ± 2	--	12 ± 2	--
2	13 ± 3	--	13 ± 3	--	8 ± 4	--	8 ± 4	--	10 ± 4	--	10 ± 4	--
3	14 ± 3	--	14 ± 3	--	16 ± 2	--	16 ± 2	--	12 ± 2	--	12 ± 2	--
4	14 ± 5	--	14 ± 5	--	17 ± 5	--	17 ± 5	--	14 ± 3	--	14 ± 3	--
5	8 ± 2	--	8 ± 2	--	9 ± 3	--	9 ± 3	--	9 ± 4	--	9 ± 4	--
6	12 ± 3	--	12 ± 3	--	15 ± 4	--	15 ± 4	--	15 ± 4	--	15 ± 4	--
7	11 ± 3	--	11 ± 3	--	Missing	--	Missing	--	11 ± 2	--	11 ± 2	--
X ± SD	12 ± 2	--	12 ± 2	--	13 ± 4	--	13[b] ± 4	--	12 ± 2	--	12 ± 2	--
[2]X ± SD	12 ± 2	--	12 ± 2	--	13 ± 4	--	13 ± 4	--	12 ± 3	--	12 ± 3	--
Experimental group												
8	11 ± 2	*	11 ± 2	0	14 ± 1	6 ± 5	20 ± 1	28	12 ± 2	0	12 ± 2	0
9	16 ± 2	*	16 ± 2	0	13 ± 3	6 ± 0	19 ± 3	31	18 ± 3	0	18 ± 3	0
10	13 ± 2	*	13 ± 2	0	10 ± 3	12 ± 0	22 ± 3	54	12 ± 2	0	12 ± 2	0
11	16 ± 6	8 ± 6[3]	24 ± 6	33	16 ± 4	5 ± 2	21 ± 4	23	14 ± 3	4 ± 2	18 ± 3	22
X ± SD	14 ± 2	2 ± 4	16 ± 5	8 ± 16	13[a] ± 2	7 ± 3	20[ab] ± 1	34 ± 14	14 ± 3	1 ± 2	15 ± 4	5 ±11

[1]Expressed in milligrams.
[2]X ± SD of subjects 2-6. Used in the paired 't' test to determine significant differences.
[3]MJ 7014 was consumed on a trial basis.
*Actual intakes recorded previous to week 1 (Appendix Table 1).
Values containing a common letter in their superscript are significantly different ($P < 0.05$).

TABLE 24

Hemoglobin and hematocrit levels.

Subject	Hemoglobin (g/100 ml)				Hematocrit (%)			
	Week				Week			
Control group	1	7-8	12-13	20	1	7-8	12-13	20
1	5.3	5.6	5.9	6.2	14.9	16.1	17.2	17.7
2	6.9	6.8	6.6	6.6	20.0	18.8	18.7	19.2
3	11.6	13.2	12.0	12.6	33.5	38.0	33.9	37.8
4	9.7	8.0	7.6	7.2	27.4	32.6	22.2	21.6
5	9.2	13.3	9.4	10.1	26.7	39.3	28.6	31.0
6	7.4	6.5	6.7	Missing	21.5	19.0	19.2	Missing
7	5.0	4.0	5.5	6.8	14.8	12.2	16.0	21.1
$\bar{X} \pm SD$	7.9±2.4	8.2±3.7	7.7±2.3	8.3±2.5	22.7±6.9	25.1±11.2	22.3±6.6	24.7±7.9
[1] $\bar{X} \pm SD$	8.0±2.6	8.5±3.9	7.9±2.5	8.3±2.5	22.9±7.6	26.2±14.9	22.8±7.1	24.7±7.9
Experimental group								
8	8.7	8.8	9.8	8.9	26.8	27.0	29.7	28.3
9	11.5	9.5	9.0	9.2	31.9	28.6	26.6	27.8
10	7.9	6.6	7.2	7.6	24.7	20.9	21.0	23.4
11	9.6	10.9	10.1	10.6	28.9	25.0	29.7	33.2
$\bar{X} \pm SD$	9.4±1.5	9.0±1.8	9.0±1.3	9.1±1.2	28.1±3.1	25.4±3.3	26.8±4.1	28.2±4.0

[1] $\bar{X} \pm SD$ of subjects 1, 2, 3, 4, 5, and 7. Used in the paired 't' test to determine significant differences.

TABLE 25

Serum iron, total iron binding capacity (T.I.B.C.), and percent saturation of serum transferrin[1] (% SST) levels.

Subject	Serum iron (ug/100 ml)				T.I.B.C. (ug/100 ml)				% SST			
	Week				Week				Week			
	1	[redacted]			7-8	12-13	20		1	7-8	12-13	20
Control group												
1	202	200	202	195	244	244	250		90	82	83	78
2	166	23	67	81	266	260	272	282	41	9	25	29
3	105	92	70	50	248	268	244	254	42	34	29	20
4	83	175	111	81	259	264	240	220	32	66	46	37
5	80	62	63	64	270	240	276	246	30	26	23	26
6	110	155	140	62	300	306	292	214	37	51	48	29
7	162	116	135	147	216	170	192	212	75	68	70	69
$\bar{X} \pm SD$	$130^{a} \pm 47$	118 ± 64	113 ± 51	$97^{a} \pm 53$	275 ± 64	250 ± 41	251 ± 33	240 ± 26	$50^{b} \pm 23$	48 ± 26	46 ± 23	$41^{b} \pm 23$
Experimental group												
8	63	187	Missing	83	300	324	Missing	336	21	58	Missing	25
9	116	155	167	190	238	226	236	238	49	69	71	80
10	Missing	196	203	134	Missing	276	292	294	Missing	71	70	46
11	39	46	47	41	232	240	212	226	17	19	22	18
$\bar{X} \pm SD$	73 ± 39	146 ± 69	139 ± 82	112 ± 64	257 ± 38	267 ± 44	247 ± 41	274 ± 51	29 ± 17	54 ± 24	54 ± 28	42 ± 28
[2]$\bar{X} \pm SD$	78 ± 54	101 ± 77	107 ± 85	116 ± 105	235 ± 4	233 ± 10	224 ± 17	232 ± 8	33 ± 23	44 ± 35	47 ± 35	49 ± 44

[1]Calculated using the formula: Serum iron (ug/100 ml) ÷ T.I.B.C. (ug/100 ml) x 100.
[2]$\bar{X} \pm SD$ of subjects 9 and 11. Used in the paired 't' test to determine significant differences.
Values containing a common letter in their superscript are significantly different ($P<0.05$).